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# STUDIES IN THE FIELD OF CONJUGATED SYSTEMS

## LXXXV. THE CONDENSATION OF DIENE HALIDES WITH ACETYLENE DICARBOXYLIC ESTER*

V. S. Miklashevskaia and A. A. Petrov

Acetylene dicarboxylic acid and its esters are among the most studied of the dienophilic compounds [1]. Among the reactions of these substances with halogen derivatives of the dienes, only the condensation with fluoroprene has been described [2].

In continuation of our studies on the diene synthesis with the participation of diene halides, we have carried out experiments on the condensation of dimethyl acetylene dicarboxylate with some chloro- and bromo-derivatives of divinyl and isoprene.

When we heated acetylene dicarboxylic ester with 1-chlorobutadiene, we could not obtain a definite condensation product.

In the case of 1-bromobutadiene we isolated only phthalic anhydride from the very small yield of a mixture which may or may not have contained halogen compounds. Thus we showed that here condensation proceeds with the splitting out of hydrogen halides. A similar reaction was found earlier when 1-halodienes were heated with ethylene dienophils [3].

Chloroprene and bromoprene gave normal condensation products with acetylene dicarboxylic ester – the dimethyl esters of 4-chloro- and 4-bromo-$\Delta^{1,4}$-dihydrophthalic acid. The first ester was a liquid, the second crystallized on standing.

Attempts to obtain the corresponding chloro- and bromodihydrophthalic acids from these esters by heating with aqueous alkali were unsuccessful. The hydrolysis was accompanied by loss of hydrogen halide and decarboxylation with formation of a mixture of benzoic and halogen containing acids. When esters of 4-fluoro-$\Delta^{1,4}$-dihydrophthalic acid and 4-halo-$\Delta^{1,4}$-dihydrobenzoic acid were saponified no appreciable loss of hydrogen halide and decarboxylation were observed [2,4].

The analogous structures of chloro- and bromoisoprene (3-chloro- and 3-bromo-2-methyl-1,3-butadiene) react with acetylene dicarboxylic ester to form dimethyl esters of 5-chloro- or 5-bromo-4-methyl-$\Delta^{1,4}$-dihydrophthalic acid. Both substances are crystalline. When they were heated with dilute alkali solutions they also lost hydrogen halides and were decarboxylated; in the case of the bromo-ester we isolated p-toluic acid.

## EXPERIMENTAL

Condensation with 1-chlorobutadiene.** 0.07 g-mole of 1-chlorobutadiene and 0.07 g-mole of dimethyl acetylene dicarboxylate (I) in 10 ml of toluene were heated in an autoclave at 130-140° for 6 hours. When the reaction product was distilled in a vacuum we obtained 5 g of the starting ester and about 1 ml of a liquid which distilled at 125-130° (10 mm), $n^{20}D$ 1.4993. Chlorine content 8.68%, OCH$_3$ content 23.14%. The substance was not further studied.

Condensation with 1-bromobutadiene. 0.06 g-mole of 1-bromobutadiene and 0.06 g-mole of ester I in 10 ml of toluene were heated in an autoclave at 160-170° for 14 hours.

Distillation of the mixture in a vacuum gave, besides the starting ester, 3.7 g of an oil boiling at 120-140° (10 mm), from which crystals of phthalic anhydride, m.p. 131°, separated on standing. Mixed m.p. 131°. The formula was confirmed by analysis.

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* Diene Compounds. LXIV. The Diene Synthesis with Participation of Diene Halides. X.

** All the diene halides were stabilized with hydroquinone.

The liquid residue was separated into two fractions: the 1st with b. p. 120-125° (10 mm), $n^{20}D$ 1.5089, contained 18.61% bromine; the 2nd with b. p. 125-130° (10 mm), $n^{20}D$ 1.5179, contained 23.04% bromine. For the expected condensation product we calculated a bromine content of 29.04%, and the boiling point could not be below 140° (10 mm) [2].

Condensation with chloroprene. 0.1 g-mole of chloroprene and 0.1 g-mole of ester I in 20 ml of toluene were heated in a sealed glass tube at 140-150° for 15 hours. We obtained 14.5 g (63%) of dimethyl 4-chloro-$\Delta^{1,4}$-dihydrophthalate.

B. p. 162-163° (10 mm), $d^{20}_4$ 1.2828, $n^{20}D$ 1.5107, $MR_D$ 53.83; calculated 53.42. Found %: Cl 15.58; $OCH_3$ 26.85. $C_{10}H_{11}O_4Cl$. Calculated %: Cl 15.37; $OCH_3$ 26.91.

0.62 g of the substance was heated in a sealed glass tube with a 10% solution of 0.54 g NaOH for 5 hours (to solution) on a boiling water bath. Then the solution was acidified with dilute nitric acid. The resulting precipitate (benzoic acid) was filtered. M. p. 120-121°. A mixed sample with commercial benzoic acid melted at the same temperature. In the filtrate we found 0.0902 g of chlorine which corresponded to 94.5% of the amount in the ester.

In another experiment, 5 g of ester and 2.6 g NaOH (10% solution) were heated under reflux for 5 hours (to solution of the ester). After acidifying with excess sulfuric acid we obtained 1.95 g of a white, crystalline substance with a diffuse melting point (123-165°) and a chlorine content of 9.32% as against 17.51% calculated for the expected acid. From 0.579 g of this mixture we steam-distilled out benzoic acid. The distillate was neutralized with NaOH. We determined 0.1172 g of benzoic acid. After evaporation and acidification we isolated benzoic acid with m. p. 120°.

0.3 g of the mixture was dissolved in 10 ml of ethyl alcohol and passed through a column of aluminum oxide for chromatography. The column of adsorbent was separated into several parts, each of which was treated separately with 0.1 N NaOH solution. The filtered liquid was acidified with sulfuric acid and extracted with ether. Thus, from the upper part of the column we obtained, apparently, 4-chlorodihydrophthalic acid with m. p. 178-181°.

Found %: Cl 16.45. $C_8H_7O_4Cl$. Calculated %: Cl 17.33.

From the lower part of the column we obtained benzoic acid by the same process.

Condensation with bromoprene. 0.1 g-mole of bromoprene and 0.1 g-mole of ester I in 10 ml of toluene were heated in a glass tube at 145° for 15 hours. The reaction product was vacuum distilled. We obtained 14.2 g (52%) of dimethyl 4-bromo-$\Delta^{1,4}$-dihydrophthalate. The substance crystallized on standing.

B. p. 164.5-165.5° (5 mm), m. p. 39-41° (from aqueous alcohol), $d^{20}_4$ 1.4876, $n^{20}D$ 1.5309.

Found %: Br 29.50; $OCH_3$ 22.02. $C_{10}H_{11}O_4Br$. Calculated %: Br 29.04; $OCH_3$ 22.56.

When the ester was saponified, we obtained benzoic acid.

Condensation with 3-chloro-2-methyl-1,3-butadiene. 0.02 g-mole of chloroisoprene and 0.02 g-mole of ester I in 10 ml of toluene were heated in a sealed glass tube at 150° for 12 hours. The reaction product was separated by distillation. It crystallized in the receiver. We obtained 2.4 g (61%) of dimethyl 5-chloro-4-methyl-$\Delta^{1,4}$-dihydrophthalic acid. Colorless tablets with m. p. 69-70° (from methyl alcohol). B.p. 170-171° (10 mm).

Found %: C 54.10, 53.90; H 5.52, 5.53; Cl 14.39, 14.24; $OCH_3$ 24.74; $C_{11}H_{13}O_4Cl$. Calculated %: C 53.99; H 5.36; Cl 14.49; $OCH_3$ 25.37.

Condensation with 3-bromo-2-methyl-1,3-butadiene. 0.07 g-mole of bromoisoprene and 0.07 g-mole of ester I in 10 ml of toluene were heated in a sealed tube at 140-150° for 12 hours. We obtained 15.7 g (77%) of dimethyl 5-bromo-4-methyl-$\Delta^{1,4}$-dihydrophthalate. Colorless needles with m. p. 73-73.5° (from methyl alcohol). B. p. 154-155° (about 3 mm).

Found %: C 46.08, 46.11; H 4.28, 4.46; Br 27.38; $OCH_3$ 21.93. $C_{11}H_{13}O_4Br$. Calculated %: C 45.69; H 4.53; Br 27.64; $OCH_3$ 21.47.

In various experiments on the hydrolysis of this ester by heating it with a 10% solution of NaOH, the content of bromide ion in the solution reached 99% of the total in the ester sample. From the hydrolytic product we isolated p-toluic acid (yield up to 60%). M. p. 178° (from water). A mixed test with commercial p-toluic acid melted at the same temperature.

## SUMMARY

1. We have studied the condensation of the dimethyl ester of acetylene dicarboxylic acid with 1-chloro- and 1-bromobutadiene, chloroprene, bromoprene, and 3-chloro- and 3-bromoisoprene.

2. In the case of the last four substances we have isolated and characterized the expected condensation products – the dimethyl esters of the corresponding halodihydrophthalic acids.

3. Phthalic anhydride was isolated from the condensation product of acetylenedicarboxylic ester with 1-bromobutadiene.

4. We have shown that the esters of 4-halodihydrophthalic acids and their homologs lose hydrogen halides and are decarboxylated when they are heated with alkali solutions.

## LITERATURE CITED

[1] Organic Reactions 4, 86 (1951).*

[2] A. A. Petrov and A. V. Tumanova, J. Gen. Chem. 26, 2995 (1956).**

[3] A. A. Petrov, Usp. Khim. 13, 203 (1944).

[4] A. A. Petrov and K. B. Rall', J. Gen. Chem. 26, 1588 (1956).**

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** Original Russian pagination. See C. B. Translation.

# STUDIES IN THE FIELD OF CONJUGATED SYSTEMS

## LXXXVI. THE COMBINATION OF PIPERYLENE HYDROCHLORIDE WITH ISOPRENE*

A. A. Petrov, N. A. Razumova, and M. L. Genusov

It was shown earlier that diene hydrocarbons react with halogen compounds in the presence of a catalyst, zinc chloride, tin chloride and others, with formation of a mixture of substances of the general formula $R-(C_nH_{2n-2})_x-X$ [1, 2]. Only saturated halogen compounds were thoroughly studied; it was shown that the rate of the reaction and the size of x depend on the nature of the alkyl halide and the structure of the diolefin. The simplest products of the combination (when x = 1) were isolated only in the case of tertiary alkyl halides and divinyl.

The investigation was continued with the study of the reaction of diene hydrocarbons with unsaturated halogen compounds of the allyl type. There was evidence in the literature of the combination of divinyl and crotyl chloride and bromide with the formation of chlorooctadienes and higher telomers [2]. We showed in our laboratory that prenyl chloride (1,4-isoprene hydrochloride) combined with isoprene to form geranyl chloride and other products [3].

In the present paper we give the results of our experiments on the combination of piperylene hydrochloride (2-chloro-3-pentene) with isoprene.

Piperylene hydrochloride is favorably distinguished from the hydrochlorides of other very simple diene hydrocarbons by the fact that both allyl isomers here have the same structure. This peculiarity of piperylene hydrochloride excludes the possibility of the participation of two isomeric forms of the hydrochloride in the reaction with the diene hydrocarbon and, hence, reduces doubly the number of possible isomeric products of the combination. The diene hydrocarbon, too, was not chosen by chance. As a result of the combination of the above hydrochloride with isoprene in the 1,4-position, we should obtain an isomer of geranyl chloride from which it would be possible to go to isomers of citral, pseudoionone, and ionone which would have practical interest.

Our experiments on the combination of 2-chloro-3-pentene and isoprene showed that the reaction proceeds in the usual way with formation of a mixture of telomers; the relative yield of the primary product of combination (at x = 1) depends chiefly on the time of contact of the reagents and the catalyst, that is, on the depth of the telomerization process. When 80% isoprene is used, the primary product of the combination and higher telomers (including dimeric halogen compounds) are obtained in a weight ratio of 1:1; when 50-35% of the isoprene is used, in a ratio of 2.5:1. However, in all these cases, the initial combination product forms in considerably greater quantity than, for example, in the reaction of prenyl chloride with isoprene.

We studied only the products of combination of piperylene hydrochloride and isoprene in 1:1 ratio. As a result of the combination of 2-chloro-3-pentene and isoprene it was possible to isolate 6 isomers with open chains and two cyclic compounds.

The actual combination products were distilled at low temperatures. The structure of the main part was established from the following data.

1) 85% of the substance reacted with formation of an aldehyde isomeric with citral in the Sommelet reaction [4]. Hence 85% of it is a primary chloride of the allyl type. The aldehyde can be obtained only from two possible products of combination of 4-chloro-2-pentene and isoprene in the 1,4- and the 4,1-positions.

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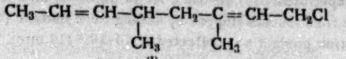
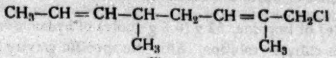
* Diene Compounds. LXV. Reaction of Dienes with Halogen Compounds. III.



$CH_3-CH=CH-\underset{CH_3}{CH}-CH_2-\underset{CH_3}{C}=CH-CH_2Cl$

(I)

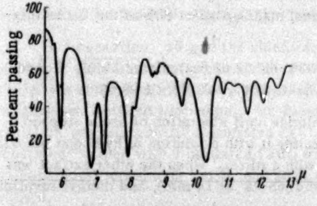


$CH_3-CH=CH-\underset{CH_3}{CH}-CH_2-CH=\underset{CH_3}{C}-CH_2Cl$

(II)

2) When the substance is split by ozone it gives acetic, chloroacetic, and methyl levulinic acids. Chloroacetone was not found. Hence formula II is excluded and there remains only formula I.

3) On hydrogenation over palladium the compound gives a saturated hydrocarbon, evidently 3,5-dimethyloctane. According to the specific gravity and refractive index it hardly differs from the form described in the literature but it has a somewhat unsharp boiling point range (2°).



Infrared spectrum of the chief fraction (NaCl prism, thickness of layer 0.1 mm).

4) The infrared spectrum of the substance (about 1.6μ and in the interval 5.5-13μ) also confirms formula I. In the spectrum there is a very intense absorption band at 970 $cm^{-1}$, which corresponds to the grouping $-CH=CH-$, and a less intense band at 864 $cm^{-1}$ which evidently corresponds to the group $R_2C=CH-$. A double bond is characterized by the frequency 1669 $cm^{-1}$ which evidently occurs because of the summation of the frequencies which lie close together and come from the two internal double bonds. The frequency 922 $cm^{-1}$ which can be related to the group $CH_2=$ appears weakly in the spectrum of the starting substance. Notable absorption characteristic of this group is also absent at 6100 $cm^{-1}$. On the other hand, after the Sommelet reaction, the spectrum of the result shows intense absorption at 906, 970, and 6100 $cm^{-1}$, characteristic for the vinyl group [5]. Hence this substance contains the product of combination of 2-chloro-3-pentene in the 1,2-position.

Thus we have shown that isoprene unites with 2-chloro-3-pentene preferably in the 1,4-position, with formation of 1-chloro-3,5-dimethylocta-2,6-diene. The 1,2-product is formed to the extent of less than 15% of the mixture of substances with the formula $C_{10}H_{17}Cl$.

This investigation has made available the above isomer of geranyl chloride, and also the isomer of citral, 3,5-dimethylocta-2,6-dienal, not previously described in the literature. The latter is a colorless oil with an odor resembling that of citral. It reacts easily with hydrazine derivatives: it gives a crystalline semicarbazone and 2,4-dinitrophenylhydrazone. When it condenses with acetone it gives an isomer of pseudoionone, 6,8-dimethylundeca-3,5,9-trien-2-one.

## EXPERIMENTAL

Piperylene hydrochloride was obtained by saturating piperylene (a mixture of cis- and trans-forms with $n^{20}D$ 1.4334) with hydrogen chloride at 0° to a weight which corresponded to about 50% conversion. The hydrochloride was purified by vacuum distillation in a Widmer column (80 mm). The yield was about 95% based on the hydrogen chloride absorbed.

B. p. 41° (100 mm), 45-46° (120 mm), $d^{20}_4$ 0.8994, $n^{20}D$ 1.4327. These constants correspond to the literature data for 4-chloro-2-pentene [6].

Telomerization was carried out in a special apparatus which allowed determination of the specific gravity of the mixture during the reaction. To a mixture of equimolecular amounts of piperylene hydrochloride and isoprene diluted with 25-50% of the weight with methylene chloride was added at 10° a 5% solution of tin chloride in methylene chloride, and the mixture was stirred at the same temperature until there was no further increase in specific gravity (determined experimentally) beyond a set value which showed that a determined depth of reaction had been reached. Then the reaction was stopped by adding diethylamine [7] and the mixture was distilled. The fraction of primary combination product was collected at 70-100° (10 mm). Under these conditions we carried out a series of experiments, some of which are described below.

a) We took 34 g (0.5 g-mole) of isoprene, 52 g (0.5 g-mole) of hydrochloride, and 30 ml of methylene chloride. We added 3 ml of 5% tin chloride solution. After the specific gravity had increased by 0.043, which took about 20 minutes, the reaction was stopped by adding 1.5 ml of diethylamine. We obtained 14.5 g of primary product and 6 g of higher telomers (including also dimers of the halogen derivatives). The depth of the transformation was about 35%.

b) With the same amounts of starting substances with an increase in specific gravity of 0.060 we obtained 27 g of primary product and 11 g of telomers. The depth of transformation was about 50%.

c) Under analogous conditions with an increase in specific gravity of 0.104 we obtained 36 g of primary product and 32 g of higher telomers. The depth of transformation was about 80%.

The primary combination products from several experiments were distilled in the Widmer column. The chief fraction (within 1°, chiefly 1-chloro-3,5-dimethylocta-2,6-diene) made up about 80% of the whole mixture. For this fraction we found:

B. p. about 64° (3 mm), 85-86° (10 mm), $d^{20}_4$ 0.9132, $n^{20}D$ 1.4730, MR 53.05; calculated 52.31. Found %: C 69.75, 69.88; H 9.94, 10.11; Cl 20.38. $C_{10}H_{17}Cl$. Calculated %: C 69.55; H 9.92; Cl 20.53.

Ozonization. 5.28 g of the substance was ozonized in ethyl chloride until absorption of ozone stopped. After the solvent was evaporated, the ozonide was decomposed by heating it with a solution of hydrogen peroxide. The decomposition product was extracted with ether in an extractor with a stirrer. When the ether extract was distilled we obtained acetic acid (30-48° at 30 mm), chloroacetic acid (68-72° at 10 mm), and methyl levulinic acid (about 135° at 9 mm).

Acetic acid was transformed into the anilide by the action of the calculated amount of thionyl chloride and then aniline. M. p. 113° (from water). A mixed melting point with a commercial sample of acetanilide showed no depression. Chloroacetic acid was isolated in the crystalline state, washed with petroleum ether, and recrystallized from the same solvent. M. p. 61-62°, confirmed by mixed melting point. Methyl levulinic acid was converted to the semicarbazone, m. p. 180-181° (from water) [8], and the 2,4-dinitrophenylhydrazone, m.p. 188-188.5° (from alcohol), which were analyzed.

Semicarbazone. Found %: N 22.78, 22.87. $C_7H_{13}O_3N_3$. Calculated %: N 22.45.

2,4-Dinitrophenylhydrazone. Found %: N 18.19, 18.24. $C_{12}H_{14}O_6N_4$. Calculated %: N 18.06.

Sommelet reaction. A preliminary determination in a small sample of the chief fraction by the method of [9] showed about 85% of primary chloride.

Then 15 g of hydrochloride in 75 ml of methylene chloride was mixed and boiled with 15 g of dry urotropin during 7 hours. The urotropin complex was extracted with two portions of water. The methylene chloride solution was separated, dried, and again treated with 10 g of urotropin for 6 hours, and then washed with water. After the methylene chloride was evaporated in a vacuum, we obtained a total of 1.5 g of residue. The water solutions of the urotropin complex were combined and gradually added to a solution of formalin with simultaneous steam distillation. The aldehyde was removed from the distillate by ether. We obtained 7.5 g (57%) of 3,5-dimethylocta-2,6-dienal.

If the reaction was carried out with urotropin by vibration in the cold for two days, the yield did not change.

B. p. 110-111° (20 mm), $d^{20}_4$ 0.8786, $n^{20}D$ 1.4830, MR 49.39 calculated 47.46.

Found %: C 79.06, 78.84; H 10.88; 10.75. $C_{10}H_{16}O$. Calculated %: C 78.90; H 10.60.

Semicarbazone: m. p. 150° (from water). White crystals.

Found %: N 19.98, 19.95. $C_{11}H_{19}ON_3$. Calculated %: N 16.86

2,4-Dinitrophenylhydrazone: orange crystals. M. p. 107° (from alcohol).

Found %: N 16.78, 16.71. $C_{16}H_{20}O_4N_4$. Calculated %: N 16.86.

The residue after the Sommelet reaction had the following properties:

B. p. 70-86° (10 mm), $d^{20}_4$ 0.9220, $n^{20}_D$ 1.4670; contained 11.5% hydrolyzed chlorine and about 76% diene compound (Kaufman method).

17 g of 3,5-dimethylocta-2,6-dienal, 32 g of acetone, and 33 ml of 10% solution of $Na_2SO_3$ were shaken in the cold for 75 hours. By vacuum distillation we obtained 14.5 g (67.5%) of a product with b. p. 139-142° (10 mm). The residue weighed 2.3 g.

6,8-Dimethylundeca-3,5,9-trien-2-one had the following constants:

B. p. 140-141° (10 mm), $d^{20}_4$ 0.8888, $n^{20}_D$ 1.5278, $MR_D$ 66.62; calculated 60.84.

Found %: C 81.30, 81.23; H 10.80, 10.74. $C_{13}H_{20}O$. Calculated %: C 81.19; H 10.48.

The semicarbazone, obtained in the usual way, had a m. p. 174-175° (from 50% alcohol).

Found %: N 16.68. $C_{14}H_{23}ON_3$. Calculated %: N 16.85.

Hydrogenation. 10 g of the chief fraction in 100 ml of methyl alcohol was hydrogenated in the presence of 40 g of palladium catalyst on calcium carbonate (with a content of 0.012 g of palladium per g of catalyst) [10]. There was absorption of 3520 ml of hydrogen (755 mm, 20°) which was 82.4% of the calculated amount. The mixture was distilled with steam. We found about 95% of the total chlorine in the sample in the residue. The distillate was diluted with a saturated $CaCl_2$ solution (to remove methyl alcohol). The hydrocarbon layer was separated, washed with a saturated $CaCl_2$ solution, a solution of potassium permanganate (to remove unsaturated hydrocarbons), dried over $CaCl_2$, and distilled in a small Widmer column. We obtained 6 g (59%) of 3,5-dimethyloctane.

B. p. 158-160°, $d^{20}_4$ 0.7151, $n^{20}_D$ 1.4132.

Literature data [11]: b. p. 160°, $d^{20}_4$ 0.7136, $n^{20}_D$ 1.4130.

## SUMMARY

1. We have studied the reaction of telomerization between piperylene hydrochloride (2-chloro-3-pentene) and isoprene in the presence of tin chloride.

2. We have shown that combination occurs chiefly in the 1,4-position, and the primary product of the reaction is preferentially 1-chloro-3,5-dimethylocta-2,6-diene.

3. The latter substance gives by the Sommelet reaction an isomer of citral: 3,5-dimethylocta-2,6-dienal. We have described its crystalline semicarbazone and 2,4-dinitrophenylhydrazone. Condensation with acetone gives an isomer of pseudoionone.

4. We have shown that hydrogenation over palladium transforms the chlorodimethyloctadiene into 3,5-dimethyloctane.

## LITERATURE CITED

[1] A. A. Petrov and K. V. Leets, J. Gen. Chem. 26, 1113 (1956)*.

[2] French patent 824909; Zbl. 1938, I, 4108.

[3] K. V. Leets Dissertation: A Study of the Combination of Alkyl Halides with Short Chain Conjugated System Compounds** LTI, (1955); Author' certificate No. 105428 (1955).

[4] R. Sommelet, C. r., 157, 852 (1913).

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* Original Russian pagination. See C. B. Translation.

** In Russian.

[5] L. J. Bellamy. The Infrared Spectra of Complex Molecules. London (1954).

[6] A. N. Pudovik and N. B. Sharipova, J. Gen. Chem. 25, 589 (1955)*.

[7] A. A. Petrov, Kh. V. Bal'ian, Iu. I. Kheruze, and E. Iu. Shvarts, Author's certificate No. 106808 (1957).

[8] I. N. Nazarov and A. N. Elizarova, Bull. Acad. Sci., Div. Chem. Sci, 1951, 295.

[9] K. V. Leets and co-workers, J. Gen. Chem. 27, 2969 (1957)*.

[10] I. Gouben. Methods of Organic Chemistry, II, ed.2, 497 (1941).

[11] F. D. Rossini, K. S. Pitzer, R. C. Arnett, R. M. Braun and G. C. Pimenter. Selected values of physical and thermodynamic properties of hydrocarbons. Pittsburg, (1953).

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# ACETYLENE DERIVATIVES

## 192. THE STEREOCHEMISTRY OF HYDROGENATION OF ACETYLENIC GLYCOLS

I. N. Nazarov*, L. D. Bergel'son, L. P. Badenkova and B. V. Lopatin**

Catalytic hydrogenation of acetylenic compounds is known to lead mainly to cis-olefins [1]. It has been often observed, however, that trans-isomers are formed at the same time, and the relative amounts appear to depend on the nature of the acetylenic compound and catalyst, and on the conditions of hydrogenation [2-14].

In connection with our investigations of the stereochemistry of addition reactions at the triple bond, it was of interest to make precise determinations of the quantities of trans-olefins formed in catalytic hydrogenation of disubstituted acetylenes and to establish whether cis-olefins undergo isomerization under hydrogenation conditions. We selected tetramethylbutynediol (2,5-dimethyl-3-hexyne-2,5-diol) and butynediol as compounds for investigation.

Stereochemistry of hydrogenation of tetramethylbutynediol. The main product of hydrogenation of tetramethylbutynediol over Pd catalyst is cis-tetramethylbutenediol with m. p. 69° [15]. The question of formation of trans-tetramethylbutenediol has hitherto remained obscure.

Zal'kind [16,17] isolated a substance with m. p. 75-76° during catalytic hydrogenation of tetramethylbutynediol; he first considered this to be the cis-isomer, but later the trans-isomer. Bourguel [10,11] assumed that the substance with m. p. 75-76° is a mixture of cis-form and "trans-isomer" which did not give a depression of melting point with the compound with m. p. 101° obtained by reduction of tetramethylbutynediol with sodium in alcohol. Later, however, Zal'kind and Bukhovets [18] established that Bourguel's "trans-form" with m. p. 101° gives a dibromide identical with the dibromide of the acetylenic glycol and breaks down with formation of acetylene when heated with caustic alkali. They therefore concluded that Bourguel's substance is a crystalline modification of tetramethylbutynediol (m. p. 95°). Data of the different authors for the geometrical isomers of tetramethylbutenediol are presented in the following table.

| Melting Points | | | Literature |
|---|---|---|---|
| 69° | 75-76° | 101° | |
| Trans | Cis | — | [19] |
| Cis | Trans | — | [20] |
| Cis | Trans-cis mixture | Trans | [10,11] |
| Cis | Trans | Acetylenic glycol | [18] [21] |
| Cis | Trans-cis mixture | Acetylenic glycol | [22] |

For the purpose of evaluating these conflicting data, it was necessary to obtain authentic specimens of pure cis- and trans-isomers of tetramethylbutenediol. We synthesized these substances from the dimethyl esters of maleic and fumaric acids.

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* Deceased.

** B. V. Lopatin carried out the stereographic part of the work.

Condensation of maleic ester with methyl magnesium bromide was effected in 1940 by Johnson [21, 22] who showed that cis-tetramethylbutenediol (m. p. 69°) was formed together with a considerable amount of the product of 1,4-addition. Johnson was unable to effect a similar condensation with fumaric ester because methyl magnesium bromide adds on to fumaric ester only in the 1,4-position even at -40°. Similar results had been obtained even earlier in a study of the reaction of fumaric ester with phenyl magnesium bromide [23].

We found that 1,4-addition can be partly prevented by the use of methyl magnesium chloride. With this reagent we obtained cis-tetramethylbutenediol with m. p. 69° from maleic ester, and trans-tetramethylbutenediol with m. p. 95-96° from fumaric ester. The latter was therefore different from all of the preparations previously assumed to be the trans-isomer. Trans-tetramethylbutenediol can be prepared by reduction of tetramethylbutynediol with lithium in liquid ammonia.

It remained to clarify the nature of the substances with m. p. 75-76° and 101° isolated by Zal'kind and Bourguel.

Bourguel's results [10,11] indicated the possibility of Zal'kind's "trans-form" with m. p. 76° actually being a molecular compound of the cis- and trans-forms. We found that a substance with m. p. 75° is easily formed when solutions of the pure cis- and trans-tetramethylbutenediols in ether are mixed. During recrystallization from ligroine it behaves like an individual compound; nevertheless, it could be resolved into the cis- and trans-forms by crystallization from water, and the pure cis-isomer is eluted (yield about 70%) by chromatography with ligroine on alumina.

The infrared spectrum of the molecular compound with m. p. 75-77° (in carbon tetrachloride) contains strong absorption bands of the associated hydroxyl groups (at 3460 $cm^{-1}$), but the bands of nonassociated hydroxyls (in the 3600 $cm^{-1}$ region) are nearly completely absent (see Fig. 1). These observations show that the complex is either a long chain of associated molecules (not fewer than ten) joined by a hydrogen bond, or consists of a cyclic structure. Comparison of the relative intensity of the bands of the cis- and trans-olefinic compounds (in the 1600 $cm^{-1}$ region), as well as data obtained during its resolution into the components, show that it contains 1 molecule of trans-tetramethylbutenediol for every 3 molecules of cis-isomer. The cis- and trans-tetramethylbutenediols are very firmly combined in the complex, as is confirmed by the presence of a very strong band of the associated hydroxyl groups even in very dilute solutions (1:10,000 in carbon tetrachloride).

Bourguel's "trans-isomer" (m. p. 101°) was likewise found to be heterogeneous. We found that this substance is formed in quantitative yields when ethereal solutions of tetramethylbutynediol (m. p. 95°) and trans-tetramethylbutenediol (m. p. 95-96°) are mixed in 1:1 ratio. Approximately the same composition of the complex is indicated by comparison of the intensity of the bands at 1662 and 1453 $cm^{-1}$ in the infrared spectra of the complex and of pure trans-tetramethylbutenediol (see Figs. 2 and 3). We see that reduction of tetramethylbutynediol under Bourguel's conditions (sodium in alcohol) does not go to completion, and we can now understand why Zal'kind succeeded in converting Bourguel's "trans-form" into an acetylenic glycol derivative.

Having obtained a supply of pure cis- and trans-isomers of tetramethylbutenediol, we were able to proceed to a study of the stereochemistry of the hydrogenation of tetramethylbutynediol.

During hydrogenation of tetramethylbutynediol over $Pd/CaCO_3$ the rate of uptake of hydrogen falls off sharply after addition of the first molecule of hydrogen (see Fig. 5).

The resulting product does not contain tetramethylbutynediol, since when heated with alkali it does not release acetylene or dimethylethynyl carbinol. Its quantitative resolution into cis- and trans-isomers by fractional crystallization and by chromatography is difficult due to the relatively small quantity of trans-isomer and the loss during recrystallization. The composition of the hydrogenated mixture was therefore determined spectrographically. As had been expected, the infrared spectrum of trans-tetramethylbutenediol contains characteristic absorption bands (at 968 and 1634 $cm^{-1}$) which are absent from the spectrum of the cis-isomer. It was impossible to directly calculate the concentrations of components in their mixture on the basis of the intensity of these bands, since a study of specially prepared mixtures of authentic composition showed that the spectra of the mixtures appreciably deviate from the Lambert-Beer law due to the formation of the molecular complex. It was therefore decided to construct calibration curves based on the intensity of the absorption bands of four mixtures of known composition (see Fig. 4). The calibration curves were plotted for the 1600 and 1400 $cm^{-1}$ regions (the plot for the 900 $cm^{-1}$ region did not give a smooth curve). Data obtained with the help of these

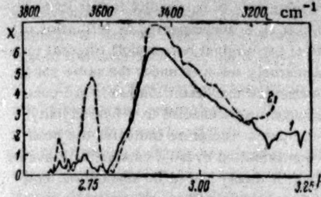


Fig. 1. Absorption spectra. 1) molecular complex of cis- and trans-tetramethylbutenediols (m. p. 75°) in the 3600-3200 $cm^{-1}$ region in $CCl_4$ at a concentration of 0.0032 g/100 ml; 2) artificially prepared mixture of cis- and trans-tetramethylbutenediols of authentic composition (17:3) in $CCl_4$ at a concentration of 0.09 g/100 ml.

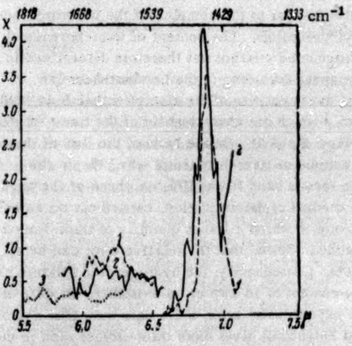


Fig. 2. Absorption spectra of cis- and trans-tetramethylbutenediols and of trans-butenediol in the 1600 $cm^{-1}$ region. 1) trans-tetramethylbutenediol in chloroform; 2) cis-tetramethylbutenediol in chloroform; 3) trans-butenediol in dioxane.

graphs showed that the product of hydrogenation of tetramethylbutynediol over Pd/$CaCO_3$ contains 84-88% of cis-tetramethylbutenediol and 12-14% of the trans-form. Since the calibration curve deviates considerably from linearity, the relative error of measurement by this method is rather large. A check on a similar mixture of known composition indicated a relative error of about 30%. The mean content of trans-tetramethylbutenediol in the hydrogenated mixture is therefore 13 ± 4%.

### Stereochemistry of the hydrogenation of butynediol.

Although the hydrogenation of butynediol has been realized on the industrial scale [24], the stereochemistry of this reaction has not been closely investigated. Romanet [2] established by fractional distillation that the product of hydrogenation of butynediol over skeletal nickel contains a considerable quantity of trans-butenediol, amounting in one case to 30%. Its content varies considerably, however, from experiment to experiment, and these results could not be reproduced. The literature is lacking in any data for the steric composition of the product of hydrogenation of butynediol over Pd catalyst. Since the stereoisomeric butenediols are liquids (the trans-isomer melts at 25°) and boil fairly closely, it appeared expedient to study the composition of the product of hydrogenation of butynediol by the spectral method. We first attempted to prepare the pure cis- and trans-butenediols needed for this determination by reduction of the dimethyl esters of maleic and fumaric acids with lithium aluminum hydride. The only product that could be isolated from this reaction, however, was saturated 1,4-butanediol. We therefore limited ourselves to the preparation in the pure form of trans-butenediol, which was synthesized by Valette's method [25] from butadiene via trans-1,4-dibromo-2-butene.

The infrared spectrum of the product of partial hydrogenation of the butynediol (absence of the band of the triple bond from the 2500-1700 $cm^{-1}$ region) shows that the first mole of hydrogen adds on to the acetylenic bond just as selectively as in the case of tetramethylbutynediol. There is a considerable difference, however, between the speeds of hydrogenation of the two acetylenic glycols. In tetramethylbutynediol the triple bond is hydrogenated very much faster that the double bond, whereas in butynediol the hydrogenation speeds up after absorption of the first mole of hydrogen (see Fig. 5). Butynediol thus behaves like acetylene, which is hydrogenated over Pd catalyst more slowly than ethylene [26].

This difference in the behaviors of butynediol and tetramethylbutynediol is probably due to steric factors. Both in butynediol and tetramethylbutynediol the triple bond is sufficiently open to allow the molecule to come close up to the catalyst. After the acetylenic derivative has been converted into an olefinic one, further hydrogenation of the molecule depends upon its approach to the catalyst from the side of a plane perpendicular to the plane of the π-bond. Inspection of models shows that such an approach is not hindered in any way in the case of ethylene and butenediol, whereas the methyl groups constitute a hindrance in the case of tetramethylbutenediol. The relatively faster absorption of the first mole of hydrogen by tetramethylbutynediol in comparison with butynediol is presumably due to the inductive effect of the methyl groups which activate the triple bond. Such an inductive effect is clearly observable in the hydrogenation of di-(p-tolyl)-butynediol, which takes up hydrogen

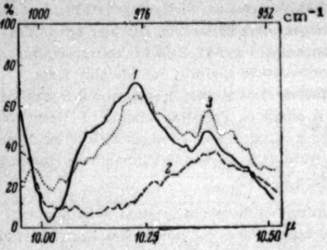


Fig. 3. Absorption spectra of cis- and trans-tetramethylbutenediols and of trans-butenediol in the 900 cm$^{-1}$ region: 1) trans-tetramethylbutenediol in chloroform; 2) cis-tetramethylbutenediol in chloroform; 3) trans-butenediol in dioxane.

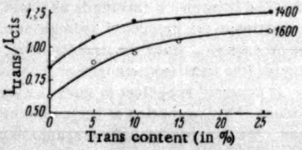


Fig. 4. Calibration graph for determination of the content of cis- and trans-tetramethylbutenediols in mixtures.

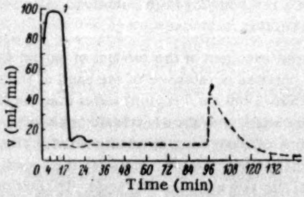


Fig. 5. Rates of hydrogenation of tetramethylbutynediol (3.32 g) and butynediol (2 g) in methanol over 10% Pd/ CaCO$_3$: 1) tetramethylbutynediol; 2) butynediol.

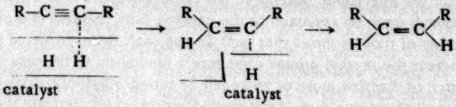
several times faster than diphenylbutynediol [27].

Another characteristic of butynediol is that its hydrogenation over Pd/ CaCO$_3$ is accompanied by formation of a resin (up to 15% of the original butynediol) whereas tetramethylbutynediol scarcely resinfies under the same conditions. At first we assumed that resinification is the consequence of isomerization of butenediol to γ-hydroxybutyraldehyde, since the patent literature indicates the possibility of such an isomerization over Pd catalyst at elevated temperature [28]. This theory had to be abandoned, however, when it was found that a still greater quantity of resin is formed on hydrogenation of butynediol diacetate. Judging by the good solubility of the resin in polar organic solvents, it is a product of partial condensation of the diacetate. By extraction with alcohol we isolated from it the dimer of butenediol diacetate with m. p. 104-105°, which had been described by Raphael [29].

Judging by the curves of the infrared spectra of pure trans-butenediol and of the product of hydrogenation of butynediol, the isomeric butenediols do not give a molecular complex similar to the complex of the stereoisomeric tetramethylbutenediols. The content of trans-butenediol in the hydrogenated mixture was therefore determined in the usual manner according to the Lambert-Beer law, on the basis of the intensities of the absorption bands at 1600 and 900 cm$^{-1}$ which are characteristic of the trans-ethylenic bond (see Figs. 2 and 3). On the basis of the first of these bands the content of trans-butenediol was 19%; on the basis of the second band it was 17%. A check of the accuracy of the method of determination, carried out on an enriched mixture to which a known quantity of trans-isomer had been added, showed that the relative error can be as much as 30%. Consequently, the hydrogenated mixture has an average content of 18 ±6% of trans-isomer. In spite of the serious experimental error, these data show that hydrogenation of butynediol gives more trans-isomer than in the case of tetramethylbutynediol. Therefore all of the preparations of butenediol which had previously been regarded as the cis-form [24, 25, 30] are actually mixtures of cis- and trans-isomers.

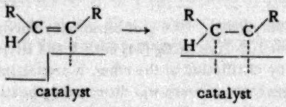
A still larger quantity of trans-form is obtained on hydrogenation of butynediol diacetate. Spectral analysis revealed a content of about 30% of trans-isomer in the product of hydrogenation.

Mechanism of formation of trans-olefinic compounds on hydrogenation. In the hydrogenation of acetylenes the semihydrogenated form does not possess free rotation, and the second hydrogen atom must add on in the cis-position.



Some authors have suggested that the trans-isomer is formed by isomerization of the cis-form in presence of the catalyst (see review [1]). Such an isomerization has never been experimentally realized (at low temperatures). It does not seem probable, since reversible isomerization must involve an equilibrium shift in the direction of the trans-form, but the quantity of trans-isomer is always small.

In connection with the hypothesis of isomerization of the cis-form, we studied the behavior of cis-tetramethylbutenediol under the conditions of hydrogenation of the triple bond. For this purpose we made use of poisoned Lindlar catalyst[31] which, as is well known, selectively reduces the triple bond to double, but is incapable of effecting hydrogenation of the olefinic bond. Cis-tetramethylbutenediol was found to be completely unchanged when shaken for a long period with this catalyst in a hydrogen atmosphere. Therefore in hydrogenation in presence of Pd catalyst the trans-glycols are not formed by isomerization of cis-butenediols. It is more probable that trans-glycols are formed in the actual hydrogenation process due to isomerization of a small portion of the semihydrogenated form at the radical with free rotation.



The free radical can be stabilized by dimerization or by polymerization, or again by transition to the trans-form.

The existence of such free radicals during hydrogenation of acetylene and methylacetylene [32] has been postulated on the evidence of formation of polymers at the same time as olefins. Formation of relatively large quantities of polymers during the hydrogenation of acetylenic glycols supports the hypothesis of the existence of a radical form of the semihydrogenated complex. In this connection it is characteristic that the quantity of trans-form increases at the same time as the quantity of polymers in the following order: tetramethylbutynediol, butynediol, butynediol diacetate.

It is reported in the literature that when acetylenes are hydrogenated with Pd catalyst poisoned by quinoline, the quantity of trans-olefin is greater than when hydrogenation is performed with unpoisoned catalyst [14]. It has even been claimed that the amount of trans-isomer depends upon the proportion of quinoline [33]. We checked these claims in a series of experiments in which tetramethylbutynediol was hydrogenated over Pd/$CaCO_3$ in presence of various quantities of quinoline. Spectral analysis showed that the composition of mixtures of tetramethylbutenediols formed under these conditions hardly differed from that of mixtures hydrogenated with unpoisoned catalyst.

## EXPERIMENTAL

Preparation of cis-tetramethylbutenediol from dimethyl maleate. A solution of 5 g of dimethyl maleate in 50 ml of absolute ether was added dropwise in the course of 2 hours, with stirring and ice-cooling, to an ethereal solution of methyl magnesium chloride prepared from 9.8 g of magnesium and 250 ml of absolute ether. The white precipitate was decomposed with saturated ammonium chloride solution. The ether layer was separated and the aqueous layer extracted with ether; the combined ethereal solutions were dried with magnesium sulfate. The ether was driven off, and the residual oil (3 g) deposited crystals when cooled; after recrystallization from ligroine (b. p. 40-60°) the crystals melted at 68-70°. Yield 0.66 g.

Fractionation of the mother liquor gave two fractions: 1st, b. p. 33.5-34° (40 mm) and 2nd, b. p. 125-140° (40 mm), $n^{21}D$ 1.4510. Freezing of the 2nd fraction (1.87 g) led to deposition of crystals with m. p. 68-69° (from ligroine). Yield 0.63 g. Total yield of cis-tetramethylbutenediol 1.3 g (15%).

Found %: C 66.33, 66.38; H 10.97, 11.16. $C_{18}H_{14}O_2$. Calculated %: C 66.62; H 11.18.

Preparation of trans-tetramethylbutenediol. a) From dimethyl fumarate. 8 g of dimethyl fumarate was condensed with methyl magnesium chloride under the same conditions as for dimethyl maleate. The reaction mixture was worked up to give two fractions: 1st with b. p. 45-100° (6-7 mm), $n^{20}D$ 1.4503; 2nd with b. p. 100-120° (1 mm), $n^{20}D$ 1.4631.

Crystals (0.65 g) came down from the 1st fraction on standing in a refrigerator; after being washed with ligroine and isooctane, they melted at 95-96°. Yield of pure trans-tetramethylbutenediol 0.5 g.

Found %: C 66.67, 66.90; H 11.06, 11.02. $C_8H_{14}O_2$. Calculated %: C 66.62; H 11.18.

b) By reduction of tetramethylbutynediol with sodium in liquid ammonia. 12 g (0.5 mole) of sodium was dissolved in 300 ml of liquid ammonia. A solution of 20 g (0.14 mole) of tetramethylbutynediol (m. p. 94.5-95.5°) in 30 g of anhydrous alcohol was then added dropwise with stirring. The reaction mixture was left overnight for evaporation of the ammonia, the residue was decomposed by stirring with 100 ml of water, the organic layer was separated, the aqueous layer was extracted with ether, and the combined extract was washed with 5% hydrochloric acid and dried with magnesium sulfate; the alcohol and ether were then distilled off. The residual crystals melted at 96-97°. Yield 14.5 g (71.7%). A mixture of these crystals with trans-tetramethylbutenediol prepared from dimethyl fumarate (m. p. 95-96°) melted without depression.

No additional quantity of the glycol could be isolated after percolation of the aqueous solution with ether for 10 hours.

Hydrogenation of tetramethylbutynediol. 17.6 g of tetramethylbutynediol in 250 ml of absolute ether was hydrogenated in presence of 0.17 g of 10% Pd/$CaCO_3$ [34] until 2.864 liters of hydrogen (18°, 743 mm) had been absorbed. After filtration followed by distillation of the ether, a crystalline product (16.4 g) was obtained with m. p. 62.5-69°. 16.4 g of the hydrogenated mixture was dissolved by heating in 200 ml of ligroine (b. p. 50-60°). Crystals with m. p. 66-70° were deposited on cooling. Three recrystallizations of these crystals from ligroine (b. p. 50-60°) led to deposition of 6.35 g of crystals with m. p. 74-75.5°.

The solvent was partly distilled off from the mother liquor. The resulting crystals melted at 63-69° after recrystallization from ligroine. Two recrystallizations of this fraction gave 3 g of crystals with m. p. 68-69°. The residual mixture of crystals (5.9 g) was fractionated in the following manner. A few portions of dilute solutions of these crystals in ligroine (b. p. 50-60°) were made up (1 g of substance in 100 ml of ligroine). After partial evaporation of the solvent at room temperature, crystals in the form of short rods (m. p. 68-69°) were separated mechanically. The residue was redissolved in ligroine. Four repetitions of this procedure followed by mechanical selection yielded 1.85 g of cis-isomer (m. p. 69°), 0.5 g of substance with m. p. 75°, and 0.17 g of trans-form (m. p. 96-97°). A mixed sample of crystals with m. p. 96-97° and trans-tetramethylbutenediol did not give a depression.

The remaining crystals were sorted into two portions – one enriched with molecular compound (1.5 g) and one enriched with cis-form (0.8 g).

The first portion was chromatographed on 25 g of alumina. Elution with ligroine (b. p. 50-60°) gave 0.45 g of cis-tetramethylbutenediol (m. p. 68-69°) and elution with benzene gave a further 0.2 g of the same product (m. p. 68-69°). Elution with a mixture of methanol and ether (1:1) gave 0.35 g of trans-tetramethylbutenediol (m. p. 95-96°). 0.1 g of substance with m. p. 74-75° was eluted with methanol.

The second portion was chromatographed on 15 g of alumina. 0.6 g of cis-tetramethylbutenediol (m. p. 68-69°) was eluted with ligroine (b. p. 50-60°), and a small quantity of trans-tetramethylbutenediol (m. p. 95-96°) with a mixture of methanol and ether (1:1). A very small quantity of substance with m. p. 75° was eluted with methanol.

Determination of the composition of a mixture of tetramethylbutenediols by the spectral method. Measurement of the spectrum of the hydrogenated mixture was carried out at two points in the 1600 $cm^{-1}$ region and at two points in the 1400 $cm^{-1}$ region. The following values of absorption coefficients ($\chi$) were obtained: $\chi_{1662}$ 1.00, $\chi_{1634}$ 0.93, $\chi_{1453}$ 3.12, $\chi_{1457}$ 3.12. The relative amounts of cis- and trans-isomers were calculated from the ratios of the respective absorption coefficients with the help of the calibration graph (Fig. 4):

$$\frac{\chi_{1662}}{\chi_{1634}} = 1.07; \ \% \text{ trans } -16; \ \% \text{ cis } -84;$$

$$\frac{\chi_{1453}}{\chi_{1457}} = 1.00; \ \% \text{ trans} -12; \ \% \text{ cis} -88.$$

The relative error of the method was estimated with the help of a specially prepared mixture containing 92.02% of cis-tetramethylbutenediol and 7.98% of trans-isomer. The following values of absorption coefficients were obtained: $\chi_{1662}$ 0.68, $\chi_{1634}$ 0.61, $\chi_{1453}$ 3.36, $\chi_{1451}$ 4.02:

$$\frac{\chi_{1662}}{\chi_{1634}} = 0.83; \ \% \ \text{trans} - 6;$$

$$\frac{\chi_{1453}}{\chi_{1451}} = 1.12; \ \% \ \text{trans} - 5.$$

The mean content of trans-isomer is 5.7%. The relative experimental error is 30%.

Preparation of the molecular compound with m. p. 74°. 0.75 g of cis-tetramethylbutenediol (m. p. 69-70°) and 0.25 g of trans-tetramethylbutenediol (m. p. 95-96°) was dissolved in absolute ether. After the ether had been driven off, the residue (1 g) had m. p. 73-74°. After recrystallization from ligroine, the crystals melted at 73.5-74° A mixture of these crystals with the substance with m. p. 74.5° obtained by hydrogenation of tetramethylbutynediol melted at 73-73.5°.

Investigation of the molecular compound with m. p. 74°. Two layers formed when the substance with m. p. 74-74.5° was heated with water. The layers were separated. Cooling of the upper layer caused crystals with m. p. 68-69° to come down (no change in melting point after recrystallization from ligroine). Evaporation of the aqueous solution in vacuo led to deposition of crystals with m. p. 73-73.5°; after recrystallization from ligroine (b. p. 35-50°), the m. p. was 74.5°. The mother liquor yielded a small quantity of crystals with m. p. 92-93° (after 3 recrystallizations from toluene). A mixed test of the crystals with m. p. 92-93° and transtetramethylbutenediol with m. p. 95-96° (obtained from dimethyl fumarate) melted at 92.5-94°.

1 g of the substance with m. p. 74-75.5° was dissolved in ligroine (b. p. 50-60°) and chromatographed on 20 g of alumina. Elution with ligroine removed 0.45 g of cis-tetramethylbutenediol (m. p. 68-69°); elution with benzene removed 0.2 g of rather less pure substance with m. p. 67-69°. Elution with 1:1 methanol/ ether and with pure methanol yielded 0.35 g of substance with m. p. 72-75°. Estimation of the composition of the molecular complex with the help of the calibration diagram (Fig. 4) gave the following values: $\chi_{1662}$ 0.62, $\chi_{1634}$ 0.55, $\chi_{1453}$ 6.94, $\chi_{1457}$ 6.22:

$$\frac{\chi_{1662}}{\chi_{1634}} = 1.13; \ \% \ \text{trans} - 27;$$

$$\frac{\chi_{1453}}{\chi_{1457}} = 1.11; \ \% \ \text{trans} - 24.$$

Preparation of the molecular complex with m. p. 101°. 0.2 g of trans-tetramethylbutenediol (m. p. 95-96°) and 0.2 g of tetramethylbutynediol (m. p. 93-94°) were dissolved in 25 ml of absolute ether. After the ether had been distilled off, the residue (0.4 g) melted at 100-101.5°. After recrystallization from ligroine (b. p. 50-60°), the crystals had m. p. 100.5-101.5°.

The composition of the complex was estimated by the spectral method on the basis of comparison of the intensities of absorption of the complex at 1662 and 1453 $\text{cm}^{-1}$ with the corresponding intensities of pure trans-tetramethylbutenediol and tetramethylbutynediol. Measurement of the spectra gave the following values of absorption coefficients:

| | $\chi_{1662}$ | $\chi_{1453}$ |
|---|---|---|
| Trans-tetramethylbutenediol | 0.75 | 3.48 |
| Tetramethylbutynediol | 0.50 | 1.78 |
| Complex | 0.55 | 2.26 |

On the basis of the Lambert-Beer law it was then calculated that the complex is made up of 38% of tetramethylbutenediol and 62% of tetramethylbutynediol.

Attempts to isomerize cis-tetramethylbutenediol. 2.5 g of cis-tetramethylbutytnediol (m. p. 69-70°) was dissolved in 60 ml of ligroine (b. p. 50-60°) and shaken for 40 hours in a hydrogen atmosphere over poisoned Lindlar catalyst [32].

Crystals with m. p. 68-70° (2.5 g) were isolated after filtration and distillation of the solvent.

Hydrogenation of tetramethylbutynediol over poisoned catalyst. To a mixture of 0.5 g of 10% Pd/CaCO$_3$, 6 ml of anhydrous methanol and 2 drops of quinoline saturated with hydrogen was added 0.5 g of tetramethylbutynediol in 6 ml of anhydrous methanol. Hydrogenation (21°, 746 mm) led to absorption of 75 ml (approx. 1 mole) of hydrogen, after which there was marked slowing down of hydrogenation. The methanol was distilled off and the residual crystals (m. p. 60-65°) were recrystallized from ligroine. Two fractions were collected: m. p. 63-66° (0.3 g) and m. p. 80-82.5° (0.14 g).

Spectral analysis of the unresolved product of hydrogenation (using the calibration graph in Fig. 4) established that it contained 6-8% of trans-tetramethylbutenediol.

Preparation of trans-2-butene-1,4-diol. This compound was synthesized by Valette's method [25]. 120 g of trans-1,4-dibromo-2-butene gave 82 g (80%) of trans-2-butene-1,4-diol diacetate (b. p. 113° (11 mm), n$^{20}$D 1.4422, m. p. 13-14.5°), which on saponification gave the trans-diol in 79% yield (b. p. 135° (13 mm), n$^{20}$D 1.4770, m. p. 25°). Trans-2-butene-1,4-diol dibenzoate melted at 98.5-100° (from alcohol). The literature gives m. p. 99-100° [30].

Hydrogenation of butynediol. A solution of 30 g of freshly distilled butynediol in 350 ml of absolute methanol was hydrogenated in presence of 3 g of 10% Pd/CaCO$_3$ until 8475 ml of hydrogen (19°, 760 mm, 9 hours) had been taken up. After filtration and distillation of the methanol, the product was distilled in vacuo. 3 fractions were collected: 1st, 60-120° (13 mm), 3 g; 2nd, 135-136° (13 mm) n$^{19}$D 1.4680, 19.3 g; 3rd, 136-141° (13 mm), n$^{19}$D 1.4678, 4 g; residue 3.6 g.

The dibenzoate of cis-2-butene-1,4-diol was obtained from the 2nd fraction; m. p. 69-70° (from alcohol); the literature reports m. p. 65-66° [30].

The composition of the mixture of butenediols was determined on the basis of the Lambert-Beer law by comparison of the intensities of the absorption bands of the mixture and of pure trans-isomer in the 1600 and 900 cm$^{-1}$ regions (see Figs. 2 and 3). The following absorption coefficients (in dioxane) were found: for pure trans-butenediol $\chi_{1677}$ 0.31; $\chi_{976}$ 5.04; for the hydrogenated mixture $\chi_{1677}$ 0.06; $\chi_{976}$ 0.86. Hence values of 19 and 17% were obtained respectively for the content of trans-isomer in the hydrogenated mixture.

Hydrogenation of butynediol diacetate. 44 g of butynediol diacetate (b. p. 106° at 13 mm, m. p. 29°) was hydrogenated in 65 ml of methanol in presence of 1.3 g of 10% Pd/CaCO$_3$; 1 mole of hydrogen (5.79 liters at 22°, 740 mm) was absorbed in 1 hour 15 minutes. After filtration and fractionation, 32 g of a mixture of cis- and trans-butenediols was obtained; b. p. 113-118° (12 mm), n$^{20}$D 1.4422; residue 8 g.

The composition of the hydrogenated mixture was determined, after the same fashion as that of the mixture of butenediols, by comparison of the intensity of the absorption band at 1626 cm$^{-1}$ (in dioxane); values of $\chi_{1626}$ 0.73 and $\chi_{1626}$ 0.25 were obtained for pure trans-butenediol acetate and the hydrogenated mixture respectively; hence the content of trans-isomer in the hydrogenated mixture was 34%. The relative error was found to be ±16% by measurements on a mixture enriched with a known quantity of the trans-form.

Reduction of dimethyl fumarate and maleate with lithium aluminum hydride. To an ethereal solution of 6.9 g of LiAlH$_4$ was added, with stirring, a solution of 8 g of dimethyl fumarate in 200 ml of absolute ether at such a rate that the ether was gently boiling (8-9 hours). Stirring was continued for 4 days at room temperature. The resulting complex was decomposed with 20% sulfuric acid. The ether layer was collected and the aqueous layer was thoroughly extracted with ether. The combined ethereal solution was dried with potassium carbonate. After the ether had been removed, a fraction with b. p. 102-104° (2 mm), n$^{19}$D 1.4612 (2.4 g) was collected; the resinous residue weighed 0.8 g. The aqueous solution was saturated with potassium carbonate until neutral, and then percolated with ethyl acetate (50 hours). 1 g of a substance with n$^{20}$D 1.4709 was isolated. A dibenzoate with m. p. 80.5-81.5° (from alcohol) was prepared from the fraction with b. p. 102-104° (2 mm).

Found %: C 72.17, 72.08; H 6.02, 6.14. $C_{18}H_{18}O_4$. Calculated %: C 72.49; H 6.07.

Under the same conditions 8 g of dimethyl maleate gave 0.75 g of a fraction with b. p. 130-138° (13 mm), $n^{20}D$ 1.4628, and 2.6 g of undistillable residue. The fraction with b. p. 130-138° (13 mm) gave a dibenzoate with m. p. 80.5-81.5° (from alcohol).

A mixture of the dibenzoates of the glycols obtained by reduction of fumaric and maleic esters melted without depression. The mixture of these dibenzoates with the dibenzoate of the butanediol (m. p. 81-82°) obtained by hydrogenation of butynediol likewise melted without depression.

## SUMMARY

1. Hydrogenation of butynediol and 2,5-dimethyl-3-hexane-2,5-diol (tetramethylbutynediol) over $Pd/CaCO_3$ converts them into mixtures of stereoisomeric olefinic glycols containing from 10 to 20% of trans-form. Hydrogenation of butynediol diacetate leads to 30 to 40% of trans-form.

2. The trans-forms are not produced by isomerization of the cis-olefinic compounds but probably with participation of free radicals during the hydrogenation; this theory is supported by the considerable polymerization that is observed during the hydrogenation of butynediol and its acetate.

3. Cis- and trans-tetramethylbutenediols form a stable crystalline complex in which the isomeric glycols are linked by a hydrogen bond. The complex is substantially undissociated in nonpolar solvents. A similar complex is formed by trans-tetramethylbutenediol with tetramethylbutynediol.

4. Tetramethylbutynediol is hydrogenated over Pd catalyst more quickly than tetramethylbutenediol, whereas butynediol absorbs hydrogen more slowly than butenediol.

## LITERATURE CITED

[1] K. N. Campbell, B. K. Campbell, Chem. Rev. 31, 77 (1942).

[2] R. Romanet, C. r. 263, 1176, 1672 (1953).

[3] F. Sondheimer, J. Chem. Soc. 1950, 877.

[4] Raman-Smets, Acad. roy. Belg., Classe sci 21, 3 (1947).

[5] A. G. Henne, K. N. Greenlee, J. Am. Chem. Soc. 65, 2020 (1943).

[6] D. E. Ames, R. E. Bowman, J. Chem. Soc. 1952, 677.

[7] I. M. Gverdtsiteli and others, J. Gen. Chem. Supp. Vol. II, 956, 960 (1953).

[8] Iu. S. Zal'kind and I. M. Gverdtsiteli, J. Gen. Chem. 9, 835 (1939).

[9] Sankichi Takei, Minoru Ono, J. Agr. Chem. Soc. Japan 18, 119 (1942); Ch. A. 1951, 4201.

[10] M. M. Bourguel and others, C. r. 180, 1753 (1925); 187, 383 (1928).

[11] M. M. Bourguel and others, Bull. Soc. chim. 45, 1067 (1929); 47, 173 (1930).

[12] M. R. Lespieau, Bull. Soc. chim. 53, 1148 (1933).

[13] Iu. S. Zal'kind and others, J. Gen. Chem. 3, 91, 573 (1933); 5, 1723 (1935).

[14] E. Ott, R. Schroter, Ber. 60, 624 (1927).

[15] A. W. Johnson, The Chemistry of the Acetylenic Compounds Vol. I, London, 191 (1946).

[16] Iu. S. Zal'kind and others, J. Russ. Chem. Soc. 48, 1830 (1916); 49, 130 (1917).

[17] Iu. S. Zal'kind and others, Ber. 56, 187 (1923); 60, 1125 (1927).

[18] Iu. S. Zal'kind and S. V. Bukhovets, J. Gen. Chem. 7, 2417 (1937).

[19] Iu. S. Zal'kind and S. A. Zaboev, J. Russ. Phys. Chem. Soc. 61, 2139 (1929).

[20] W. A. Roth, Fr. Muller, Ber. 60, 643 (1927).

[21] J. R. Johnson, J. Am. Chem. Soc. 63, 2282 (1941).

[22] J. R. Johnson, O. H. Johnson, J. Am. Chem. Soc. 62, 2615 (1940).

[23] Th. Purdie, P. Arup, J. Chem. Soc. 1910, 1537.

[24] W. Reppe, Lieb. Ann. 596, 1 (1955).

[25] A. Valette, Ann. Chim. 3 (12), 644 (1948).

[26] Tamaru, Bull. Chem. Soc. Japan 23, 64 (1950).

[27] A. I. Nogaidell, J. Gen. Chem. Supp. Vol. II, 1629 (1953).

[28] German Patent 717062; Chem. Abs. 38, 2343, 2344 (1944).

[29] R. A. Raphael, J. Chem. Soc. 1952, 401.

[30] C. S. Marvel, Ch. H. Young, J. Am. Chem. Soc. 73, 1066 (1951).

[31] H. Lindlar, Helv. Chim. Acta 35, 446 (1952).

[32] G. C. Bond. Catalysis, Vol. 3, 109 (1955).

[33] A. Mondon, Lieb. Ann. 577, 181 (1952).

[34] M. Busch, H. Stove, Ber. 49, 1064 (1916).

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# INVESTIGATION OF THE VAPOR-PHASE CATALYTIC HYDRATION OF ACETYLENE AND ITS DERIVATIVES

## II. HYDRATION OF ETHYNYLBENZENE, TERT. BUTYLACETYLENE, DIMETHYLACETYLENE, METHYLETHYLACETYLENE AND ETHYLVINYLACETYLENE

Iu. A. Gorin and L. P. Bogdanova

Hydration of mono- and disubstituted acetylenes leads to formation of ketones. These reactions (like the reaction with acetylene) are realized in the liquid phase in presence of mercury salts. Mowat and Smith [1] added water to 2-pentyne in presence of mercuric sulfate and obtained a mixture of diethyl and methyl propyl ketones. Hennion and others [2] hydrated 1-hexyne, 1-octyne, 1-heptyne and dibutylacetylene in aqueous solutions of methanol or acetone in presence of $HgSO_4$. The reaction products were the corresponding ketones. I. N. Nazarov [3] performed the hydration of hydrocarbons of the divinylacetylenic series. Sherrill and Smith [4] hydrated 9,10-undecynoic acid and obtained a mixture of two ketoacids. E. D. Venus-Danilova and S. N. Danilov [5] hydrated primary acetylenic alcohols.

Hydration of acetylenic derivatives in aqueous solutions in presence of mercuric sulfate usually proceeds satisfactorily if the acetylenic compound or the product of its hydration is soluble in water. The method does not usually give good results if the compounds are insoluble in water.

In our preceding communication [6] we presented the results obtained for hydration of vinylacetylene on solid catalysts not containing mercury compounds. In the present work we investigated the possibility of hydration of other mono- and disubstituted derivatives of acetylene over cadmium-calcium phosphate catalyst. We showed that this simple method is a route from acetylenic derivatives to ketones of various structures. Vapor-phase hydration proceeds extremely effectively with monosubstituted acetylenic derivatives. The process proceeds less intensively with disubstituted derivatives, presumably due to the special features of their structure which results in reaction at lower velocities and with lower yields of hydration products – ketones.

Pyrolysis of methane to acetylene is accompanied by formation of small quantities of substituted acetylenes. In connection with the projected industrial realization of such processes (for acetylene manufacture) in our country, the possibility may arise of certain acetylene derivatives becoming accessible products which might serve as starting substances for ketones.

Our investigations of the hydration of various acetylenic hydrocarbons over cadmium-calcium phosphate catalyst enable us to arrange them in order of activity (expressed as degree of transformation of the hydrocarbons under uniform experimental conditions: space velocity 100 l/l cat. hr., temperature 375°, and hydrocarbon/water ratio 1:10). These data are presented in Table 1.

The table indicates that the degree of transformation of a monosubstituted acetylenic hydrocarbon depends on the nature of the radical at the acetylenic bond. Acetylene is intermediate between ethynylbenzene and tert.-butylacetylene in respect of activity during hydration in the vapor phase. Substituting groups may be arranged in the following order in respect of their effect on the triple bond:

$$C_6H_5- > (CH_3)_3C- > CH_2=CH-.$$

The degree of transformation of disubstituted derivatives is nearly one-half of that of monosubstituted derivatives.

**TABLE 1**

Comparison of Activity of Hydrocarbons of the Acetylenic Series During Vapor-Phase Hydration over Cadmium-Calcium Phosphate Catalyst

| Name | | Degree of transformation of hydrocarbon % | Yield of carbonyl compounds, as mole-% of reacted hydrocarbon |
|---|---|---|---|
| of acetylenic hydrocarbon | of carbonyl compound obtained | | |
| Ethynylbenzene | Acetophenone | 76.0 | 64.0 |
| Acetylene | Acetaldehyde | 71.0 | 67.0 |
| Tert.-butylacetylene | Pinacoline (3,3-dimethyl-2-butanone) | 64.0 | 75.0 |
| Vinylacetylene | Methyl vinyl ketone | 36.5 | 70.5 |
| Dimethylacetylene | Methyl ethyl ketone | 38.5 | 37.2 |
| Methylethylacetylene | Mixture of methyl propyl ketone and diethyl ketone | 34.3 | 35.0 |
| Ethylvinylacetylene | Ethyl propenyl ketone | 21.8 | 40.4 |

On the basis of the previously enunciated ideas [7, 8] about the nature of the interaction of acetylene with the copper ion, we put forward a mechanism of the hydration of acetylene and acetylenic hydrocarbons over solid, ionic catalysts that accounts broadly for the activation of the acetylenic molecule and its action on water. This mechanism is based on the concept of interaction of the acetylenic molecule with elements of the lattice, leading to polarization of the acetylene and to formation of a complex. According to the literature [9], and in the light of the results of Iu. A. Gorin and I. K. Gorn [10], various salts and oxides of cadmium, copper and zinc are catalysts for the hydration of acetylene. We therefore assume that cations of these metals serve as the activating agent in the present case.

We shall now consider the hydration of acetylene in presence of cadmium-calcium phosphate catalyst. We designate by $Cd^+$ the cation of the cadmium phosphate lattice* that acts on acetylene (making the assumption that it has a definite positive charge whose magnitude depends on the degree of ionization of the atoms and atomic groups in the crystal lattice [11]). Adsorption of a molecule of acetylene on the surface of the catalyst causes it to fall into the sphere of action of a cadmium ion so that it becomes polarized, the $\pi$-electron of the triple bond being shifted toward the positively charged cation of the lattice ($Cd^+$). This interaction of polarized acetylene molecules and $Cd^+$ leads to formation of a complex with a positive charge at one of the carbon atoms:

$$CH\equiv CH + Cd^+ \longrightarrow \overset{\delta^+}{C}H \overset{\frown}{\equiv} \overset{\delta^-}{C}H + Cd^+ \longrightarrow \overset{\delta^+}{C}H = CH \dashrightarrow Cd$$

The broken arrow designates a bond in the complex formed at the expense of transfer of electrons from a polarized acetylenic molecule to a positively charged cadmium ion. A molecule of water is also adsorbed by the surface of the catalyst and its degree of polarization increases under the influence of lattice ions. A polarized molecule of water reacts with the polar complex, forming vinyl alcohol which further isomerizes to acetaldehyde. During this stage the lattice cation is regenerated**.

$$Cd \dashleftarrow CH = \overset{\delta+}{C}H + HOH \longrightarrow Cd^+ + CH_2 = CHOH \longrightarrow CH_3CHO$$

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* According to [12] calcium phosphate does not catalyze the hydration of acetylene, and it only functions as a carrier in presence of copper and cadmium phosphates.

** The results of the present work, including the mechanism of hydration of acetylene and its derivatives over cadmium-calcium phosphate catalyst, were submitted on December 3, 1956 to the Scientific Council of the All-Union Scientific Research Institute for Synthetic Rubber (see protocol no. 19). On January 11, 1957 the All-Union Institute received a manuscript from E. N. Tsybina, A. I. Gel'bshtein and M. I. Temkin in which the authors submit a mechanism basically similar to ours for the hydration of acetylene over a zinc phosphate catalyst.

The hydration of acetylenic derivatives over solid catalysts proceeds according to a mechanism that should not differ from the mechanism of hydration of acetylene. In the present case, however, unsymmetrical molecules of acetylenic derivatives must differ from acetylene in possessing a certain polarity due to the influence of substituents. This influence accounts for the presence of a dipole moment in compounds of the type in question [13]. The distribution of the electronic density may be represented by the following scheme for monosubstituted acetylenic hydrocarbons:

$$(CH_3)_3C-\overset{\delta^+}{C}\equiv\overset{\delta^-}{C} + Cd^+ \longrightarrow (CH_3)_3C-\overset{\delta^+}{C}=CH \dashrightarrow Cd$$

In the reaction of a water molecule with the polar complex, the negatively charged hydroxyl group adds on to the positively charged carbon atom:

$$(CH_3)_3C-\overset{\delta+}{C}=CH \dashrightarrow Cd + HOH \longrightarrow Cd^+ + (CH_3)_3C-COH=CH_2 \rightarrow$$
$$\rightarrow (CH_3)_3C-CO-CH_3$$

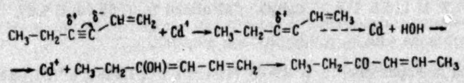
It follows from the data of Table 1 that acetylene and its derivatives (ethynylbenzene and tert.-butylacetylene) differ from one another in degree of transformation, but this difference is relatively small. The substituent at the triple bond probably creates a steric hindrance to the hydration of monosubstituted acetylenic hydrocarbons; the inhibiting effect of the steric factor may, however, be offset by the influence of the substituent and by the degree of polarity and polarizability of the acetylenic hydrocarbon. For this reason the rates of hydration of monosubstituted derivatives generally do not differ greatly from the rate of hydration of acetylene. The considerable difference in the degree of transformation during hydration of vinylacetylene may be explained by the effect of conjugation of the double and triple bonds which equalizes the electronic density and lowers the degree of polarization of the acetylenic bond.

The rate of transformation of disubstituted acetylenic hydrocarbons is approximately half that of the rate of transformation of monosubstituted acetylenes. It is highly probable that steric hindrance is responsible for this inhibition in presence of two substituent groups.

Two substituents at the triple bond may influence not only the reaction rate (which determines the degree of transformation) but also the structure and composition of the products obtained. A hydroxyl group may join on at the triple bond of a disubstituted acetylenic hydrocarbon at either the $\alpha$ or the $\beta$ carbon atom:

$$R-\underset{\alpha}{C}\equiv\underset{\beta}{C}-R_1$$

If R and $R_1$ are the same, a single product is obtained by hydration. If they are different, the direction of the reaction will evidently be governed by the competing influence of the substituents. The amounts of isomers formed will be approximately equal when there is little difference in the actions of the two groups. Hydration of methylethylacetylene, for example, leads to two isomers – diethyl ketone and methyl propyl ketone. But if the radicals are very unequal in activity, then only one product will be formed. An example is ethylvinylacetylene, hydration of which gives only ethyl propenyl ketone. We assume that the enol form is an intermediate in this reaction and subsequently isomerizes to ethyl propenyl ketone:



An alternative explanation of the formation of ethyl propenyl ketone involves a considerable shift of the electron density along the conjugated chain towards the enol group (due to the polarizing effect of the ethyl radical [14]), the addition of the elements of water in the 1-4 position, and isomerization of the intermediately formed allenic enol form:

$$CH_3-CH_2-\overset{\delta^+}{C}\equiv C-CH=\overset{\delta^-}{CH_2} + Cd^+ \longrightarrow CH_3-CH_2-\overset{\delta^+}{C}=C=CH-CH_2 \dashrightarrow Cd + HOH \longrightarrow$$
$$\longrightarrow Cd^+ + CH_3CH_2C(OH)=C=CH-CH_3 \longrightarrow CH_3-CH_2COCH=CH-CH_3 .$$

No absolute proof has of course been obtained as yet of our proposed mechanisms. It is necessary to carry out further investigations of the behavior of other representatives of the acetylenic hydrocarbon series during hydration in the vapor phase. It should then be possible to obtain ample data to establish the validity or otherwise of the concepts here put forward.

## EXPERIMENTAL

### Substances, Apparatus, and Experimental Procedure

Dimethylacetylene was prepared by cleavage (with alcoholic alkali) of hydrogen chloride from 2,2-dichlorobutane; the latter was obtained by chlorination of methyl ethyl ketone with $PCl_5$ by the procedure of A. E. Favorskii [15]. B. p. 27-27.2°, $d^{20}_4$ 0.7128, $n^{25}D$ 1.3891.

Ethynylbenzene* with b. p. 142-143°, $d^{12}_4$ 0.9368, $n^{17}D$ 1.5503.

Tert.-butylacetylene was prepared by removing hydrogen chloride (with alcoholic alkali) from 2,2-dichloro-3-methylbutane. B. p. 39.5°, $d^{15}_4$ 0.6732, $n^{15}D$ 1.3772.

Methylethylacetylene was prepared by removing hydrogen chloride from 3,3-dichloropentane. B. p. 56-56.5°, $d^{17}_4$ 0.7121, $n^{20}D$ 1.4042.

Ethylvinylacetylene** was prepared by the method of Carothers [16]. B. p. 83.5-84.0°, $d^{20}_4$ 0.7479, $n^{20}D$ 1.4522.

Acetylene was obtained from a cylinder. It was purified by passage through sodium hypochlorite solution before entering the converter.

Vinylacetylene. The commercial product was used (obtained by dimerization of acetylene).

Catalyst. A mixture of cadmium and calcium phosphates was prepared from a mixture of cadmium nitrate and calcium acetate solutions by precipitation with ammonium phosphate [17]. The precipitate was washed and dried at 110°. Tablets were prepared from the powder in a laboratory hydraulic press.

Hydration of the liquid hydrocarbons was undertaken in a quartz tube filled with the catalyst (10 ml) and placed in an electric furnace. The reaction temperature was measured with a thermocouple. Liquid hydrocarbon and water were proportioned from burets; the buret containing the hydrocarbon was cooled with ice. The reaction products were passed through a condenser and collected in a receiver which was also cooled with ice or a mixture of ice and salt (depending upon the boiling point of the original hydrocarbon). Each experiment extended over 1.5 hours. After an experiment the catalyst was regenerated in a mixture of air and steam at 450°.

### Hydration of Hydrocarbons

Hydration of ethynylbenzene. The liquid products consisted of two layers – aqueous and oily. The layers were separated, and the quantity of carbonyl compounds was determined in the aqueous layer by reaction with hydroxylamine hydrochloride. The oily layer was fractionally distilled to give two fractions: 1st with b. p. 49-50° (14 mm), $n^{17}D$ 1.5500 (unreacted ethynylbenzene); 2nd, b. p. 83-85° (12 mm), acetophenone; $d^{25}_4$ 1.0229, $n^{20}D$ 1.5339.

Found %: C 80.9; H 7.2. M 116.5, 118.5. $C_8H_8O$. Calculated %: C 80.00; H 6.67. M 120.

Acetophenone semicarbazone with m. p. 196-197° was prepared.

Literature data [18] for acetophenone: b. p. 83-85° (12 mm), $d^{25}_4$ 1.0236, $n^{20}D$ 1.5342; semicarbazone m. p. 195-198°.

Hydration of tert.-butylacetylene. Fractional distillation of the condensate gave two fractions: 1st, b. p. 39.5°, $n^{15}D$ 1.3770 (unreacted tert.-butylacetylene); 2nd, an azeotrope of 3,3-dimethyl-2-butanone with water, boiling at 85°. The azeotrope was dried with calcium chloride and redistilled to give 3,3-dimethyl-2-butanone with b. p. 102-104°, $d^{20}_4$ 0.8017.

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* Obtained from T. A. Favorskaia.

** Obtained from A. A. Petrov.

Found %: C 72.21; H 12.43. M 97.5. $C_6H_{12}O$. Calculated %: C 72.0; H 12.0. M 100.

3,3-Dimethyl-2-butanone oxime with m. p. 74.5-75° was prepared.

Literature data [19a] for 3,3-dimethyl-2-butanone: b. p. 102-104°, $d^{20}_4$ 0.7999; oxime, m. p. 74.5-75°.

Hydration of dimethylacetylene. Fractional distillation of the reaction products gave: 1st b. p. 27-27.2° (unreacted dimethylacetylene); 2nd, b. p. 72-73° – azeotrope of methyl ethyl ketone with water. The azeotrope was dried with calcium chloride and the product was again fractionally distilled to give methyl ethyl ketone.

B. p. 80°, $d^{20}_4$ 0.8051, $n^{20}D$ 1.3782. M 71.5, 72.0. $C_4H_8O$. Calculated: M 72.0.

The semicarbazone of methyl ethyl ketone with m. p. 139-140° was prepared.

Found %: 46.55, 46.26; H 8.81, 8.82. $C_5H_{11}ON_3$. Calculated %: C 46.51; H 8.52.

Literature data [19b] for methyl ethyl ketone: b. p. 80°, $d^{20}_4$ 0.8058, $n^{20}D$ 1.3788; semicarbazone with m. p. 140°.

Hydration of methylethylacetylene. Fractional distillation of the liquid products gave the following fractions: 1st, b. p. 56-56.5°, $n^{20}D$ 1.4041 (unreacted methylethylacetylene); 2nd, b. p. 82-82.9°, azeotrope of the ketones formed in the reaction and water. After drying with calcium chloride, the product was redistilled and a fraction with b. p. 101.5-102°, $d^{20}_4$ 0.8106, $n^{20}D$ 1.3901 was isolated.

Found %: C 70.53, 69.93; H 11.83, 11.32. M 82.8, 83.1. $C_5H_{10}O$. Calculated %: C 69.76; H 11.63. M 86.

The semicarbazone of the ketones was prepared; after numerous recrystallizations from alcohol it melted at 83°.

Literature data [19, c,d] for diethyl ketone: b. p. 101.5-102°, $d^{20}_4$ 0.8159, $n^{20}D$ 1.3922; semicarbazone with m. p. 139°. For methyl propyl ketone: b. p. 102°, $d^{20}_4$ 0.8089, $n^{20}D$ 1.3894; semicarbazone m. p. 110°.

The product of hydration of methylethylacetylene is evidently a mixture of two isomeric ketones. The elementary composition of the mixture and its molecular weight correspond to each of the isomers. The densities and refractions of the mixture are intermediate between the values for each of the isomers. The melting point of the mixture of the semicarbazones of the ketones is lower than the melting point of either substance separately.

Hydration of ethylvinylacetylene. The carbonyl compounds were extracted from the condensate with ligroine. A ketone was isolated on distillation of the ethereal extract.

B. p. 35-36° (10 mm), $d^{20}_4$ 1.8543, $n^{20}D$ 1.4384; semicarbazone m. p. 157-160°.

Due to the speed of polymerization of the ketone and its small quantity, it was impossible to determine its boiling point at atmospheric pressure. Comparison with the literature data indicates that the product is ethyl propenyl ketone. A scheme for its formation was given previously.

Literature data [19e] for ethyl propenyl ketone: b. p. 140-140.6°, $d^{20}_4$ 0.8558, $n^{20}D$ 1.4391; semicarbazone m. p. 160°.

Hydration of acetylene and vinylacetylene was effected by the procedure described in the preceding communication [6]. Acetaldehyde in the product of hydration of acetylene, and methyl vinyl ketone in the product of hydration of vinylacetylene were determined with the help of hydroxylamine hydrochloride. The proportion of unreacted hydrocarbons was determined from the content of unsaturated compounds in the exit gas.

Mean values from three to four parallel experiments (degree of transformation of the acetylenic hydrocarbon and yield of carbonyl compounds) are presented in Table 1.

We extend our profound thanks to T. A. Favorskaia and A. A. Petrov for provision of ethynylbenzene and ethylvinylacetylene.

## SUMMARY

1. A study was made of the hydration of some mono- and disubstituted acetylene homologs over cadmium-calcium phosphate catalyst in the vapor phase.

2. The degrees of transformation of some monosubstituted acetylenes during vapor-phase hydration over solid catalyst under identical experimental conditions were compared. It was established that their activity depends on the nature of the radical at the triple bond.

3. Under the same conditions disubstituted acetylenes are hydrated more slowly than monosubstituted derivatives.

4. Schemes are proposed for the process of hydration of acetylene and its derivatives over solid catalysts in the vapor phase.

## LITERATURE CITED

[1] E. L. Mowat, I. C. Smith, J. Chem. Soc. 1938, 19.

[2] L. E. Hennion, J. Am. Chem. Soc. 60, 718 (1938).

[3] I. N. Nazarov, Prog. Chem. 14, 41 (1945).

[4] M. L. Sherrill, I. C. Smith, J. Chem. Soc. 1937, 1501.

[5] E. D. Venus-Danilova and S. N. Danilov, J. Gen. Chem. 2, 145 (1932).

[6] Iu. A. Gorin and L. P. Bogdanova, J. Gen. Chem. 28, 657 (1958).*

[7] Z. F. Dobler, Dissertation: Study of the Polymerization of Acetylene in Solution in CuCl · MCl and the Role of Complex Compounds in this Process [In Russian] (All-Union Scientific Research Institute for Synthetic Rubber, 1954).

[8] A. L. Klebanskii, I. M. Dolgopol'skii and Z. F. Dobler, Proc. Acad. Sci. USSR 114, 323 (1957).*

[9] W. I. Tapp, Ind. Eng. Ch. 44, 2020 (1952); I. L. Kotliarevskii, Catalytic Hydrogenation [In Russian] (Acad. Sci. USSR Press 1956), p. 58.

[10] Iu. A. Gorin and I. K. Gorn, Report of the All-Union Scientific Research Institute of the Synthetic Rubber Industry [In Russian] 1954.

[11] A. F. Wells, Structure of Inorganic Substances [Russian translation] (Foreign Lit. Press 1948).

[12] Iu. A. Gorin, V. M. Svetozarova and I. K. Gorn, Report of the All-Union Institute of Scientific Research of the Synthetic Rubber Industry (1953).

[13] C. F. Smyth, Dielectric Constants and the Structure of Molecules [Russian translation] (United Sci. Tech. Press 1937).

[14] A. A. Petrov and Iu. I. Porfir'eva, J. Gen. Chem. 23, 1867 (1953).*

[15] A. Favorski, J. pr. Ch. 37, 393 (1888).

[16] W. H. Carothers, A. Jacobson, J. Am. Chem. Soc. 54, 4070 (1932).

[17] Iu. A. Gorin and A. N. Makashina, Report of the All-Union Sci. Res. Inst. for Synthetic Rubber (1954-1955).

[18] Beilst. 7, 271 (1925).

[19] Dict. Org. Compounds [Russian translation] (Foreign Lit. Press, 1949).

a) III, p. 443; b) II, p. 647; c) I, p. 795; d) II, p. 800; e) II, p. 186.

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# THE MECHANISM OF THE CATALYTIC ACTION OF ALUMINUM CHLORIDE

## VI. MORE ABOUT THE KINETICS AND MECHANISM OF THE ALKYLATION OF BENZENE WITH CHLORO DERIVATIVES

N. N. Lebedev

After one of our previous communications [1] had been printed, we had the opportunity of seeing the paper by Brown and Grayson [2] on the kinetics of alkylation of benzene with some halogenated compounds in the same solvent – nitrobenzene. They confirmed that the reaction was monomolecular with respect to the halogen compound and the aromatic compound, but their results were markedly different from ours for the order of reaction with respect to aluminum chloride and concerning the influence of the solvent. In the above authors' experiments, replacement of 60% of the nitrobenzene by methylcyclohexanone or benzene did not have a serious effect on the reaction rate, which was proportional to the concentration of aluminum chloride. We decided to make a more extensive investigation of this reaction in view of the necessity for explaining the wide discrepancy between the results of Brown and Grayson and our own, and also in view of the great importance of these results for generalization of the mechanism of the reaction.

Starting substances and experimental technique. The chloro compounds used in this work were cyclohexyl chloride (b. p. 142.5-143°, $n^{20}D$ 1.4612), tert. butyl chloride (b. p. 51.5-52°, $n^{20}D$ 1.3900), and tert. amyl chloride (b. p. 85-86°, $n^{20}D$ 1.4059). They were prepared from the corresponding alcohols and hydrochloric acid; the products were twice distilled through a column, and the middle cuts were collected. Employment of nitrobenzene as solvent for aluminum chloride and homogenization of the reaction mass enabled us to use solvents (apart from benzene, nitrobenzene and carbon disulfide) in the shape of rather less active chloro derivatives that do not react with benzene under these conditions (1,2-dichloroethane, 1,1,2,2-tetrachloroethane and carbon tetrachloride). The latter were purified with concentrated sulfuric acid and distilled from a column; middle cuts boiling in a range of 0.5-1° were collected. The carbon disulfide was purified with mercury. Purification methods and the quality of the benzene were the same as before [1].

The reaction mass was prepared from appropriate volumes of nitrobenzene, 10% aluminum chloride solution in nitrobenzene, solvent and benzene. The quantity of alkyl chloride taken was always such that its starting concentration was 0.200 mole/liter. In order to avoid polyalkylations, the benzene was always used in 7-8-fold excess in relation to the halogen compound. The previously described procedure [1] for estimation of the quantity of hydrogen chloride formed was applied in order to follow the course of the reactions. The data for solubility of hydrogen chloride in carbon tetrachloride, carbon disulfide, and dichloro- and tetrachloroethane, required for these observations, were determined by holding the solutions in a thermostat for 4 hours at the required temperature and by subsequent titration of the hydrogen halide present in the liquid and gas phases. (These data had previously been obtained for benzene and nitrobenzene [1].) Results are presented in Table 1. The values for carbon tetrachloride, dichloroethane and tetrachloroethane are 10-20% lower than those reported by Bell [3], probably because we used fairly anhydrous substances.

Reaction order with respect to aluminum chloride. With the objective of confirming our earlier data for a mixed solvent comprising benzene and nitrobenzene [1], we carried out a similar investigation for a mixture of nitrobenzene and carbon tetrachloride, using tert. butyl and amyl chlorides as alkylating agents (Tables 2 and 3). Experiments were run at 20 ± 0.05° and with a benzene concentration of 12.5 vol.-%.

TABLE 1

| Number | Solvent and temperature | Concentration of HCl (moles) | | Solubility $\alpha$ | |
|---|---|---|---|---|---|
| | | solution | gas phase | | |
| 1 | 1,2-Dichloroethane, 20° | 0.169 | 0.0142 | 11.90 | 11.85 |
| 2 | | 0.218 | 0.0187 | 11.67 | |
| 3 | | 0.097 | 0.0081 | 11.97 | |
| 4 | 1,2-Dichloroethane, 40° | 0.078 | 0.0101 | 7.72 | 7.8 |
| 5 | | 0.136 | 0.0174 | 7.82 | |
| 6 | Carbon tetrachloride, 20° | 0.0294 | 0.0078 | 3.77 | 3.85 |
| 7 | | 0.0923 | 0.0233 | 3.96 | |
| 8 | | 0.0544 | 0.0142 | 3.83 | |
| 9 | Carbon tetrachloride, 10° | 0.0393 | 0.0095 | 4.14 | 4.15 |
| 10 | | 0.0624 | 0.0150 | 4.17 | |
| 11 | 1,1,2,2-Tetrachloroethane, 20° | 0.0772 | 0.0140 | 5.51 | 5.5 |
| 12 | | 0.0489 | 0.0089 | 5.49 | |
| 13 | 1,1,2,2-Tetrachloroethane, 10° | 0.110 | 0.0179 | 6.14 | 6.0 |
| 14 | | 0.076 | 0.0130 | 5.84 | |
| 15 | Carbon disulfide, 20° | 0.0442 | 0.0076 | 5.82 | 5.85 |
| 16 | | 0.0674 | 0.0115 | 5.87 | |
| 17 | Carbon disulfide, 10° | 0.135 | 0.0164 | 8.23 | 8.1 |
| 18 | | 0.097 | 0.0122 | 7.95 | |

TABLE 2

Reaction of Tert. Butyl Chloride with Benzene

| Concentration of aluminum chloride (moles) | Composition of medium (vol-%) | | Number of parallel experiments | Velocity constant $\kappa_1$ (min $^{-1}$) | Order of reaction with respect to $AlCl_3$ |
|---|---|---|---|---|---|
| | $CCl_4$ | nitrobenzene | | | |
| 0.203 | 60.3 | 25.0 | 5 | 0.055 ± 1.4% | 1.68 |
| 0.100 | 60.3 | 25.0 | 3 | 0.0167 ± 1.55% | |
| 0.203 | 48.0 | 37.5 | 4 | 0.146 ± 2.3% | 1.33 |
| 0.100 | 48.0 | 37.5 | 4 | 0.057 ± 0.6% | |
| 0.100 | 35.5 | 50.0 | 3 | 0.202 ± 2.05% | 1.12 |
| 0.049 | 35.5 | 50.0 | 4 | 0.091 ± 1.4% | |

TABLE 3

Reaction of Tert. Amyl Chloride with Benzene

| Concentration of aluminum chloride (moles) | Composition of medium (vol-%) | | Number of parallel experiments | Velocity constant $\kappa_1$ (min $^{-1}$) | Order of reaction with respect to $AlCl_3$ |
|---|---|---|---|---|---|
| | $CCl_4$ | nitrobenzene | | | |
| 0.203 | 35.5 | 50.0 | 4 | 0.121 ± 2.5% | 0.93 |
| 0.100 | 35.5 | 50.0 | 3 | 0.063 ± 1.4% | |
| 0.100 | 23.0 | 62.5 | 5 | 0.179 ± 3.0% | 0.85 |
| 0.049 | 23.0 | 62.5 | 4 | 0.098 ± 1.4% | |
| 0.049 | 10.5 | 75.0 | 4 | 0.255 ± 3.7% | 0.77 |
| 0.025 | 10.5 | 75.0 | 4 | 0.147 ± 1.25% | |

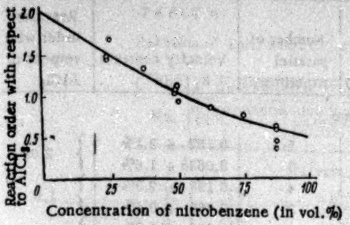


Fig. 1. Dependence of the reaction order with respect to aluminum chloride on the concentration of the solvent.

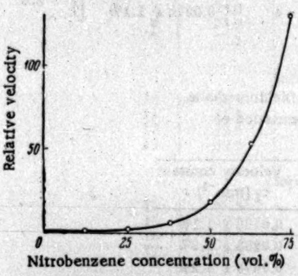


Fig. 2. Velocity of alkylation as a function of the concentration of the solvent.

These examples therefore also confirm that the order of reaction with respect to aluminum chloride decreases with increasing content of nitrobenzene in the reaction mass. All of the data obtained for the mixed solvents benzene-nitrobenzene [1] and carbon tetrachloride-nitrobenzene are plotted in Fig. 1. They vividly demonstrate the variability of the order of reaction with respect to aluminum chloride in dependence on the properties of the solvent, changing from 0.5 for nitrobenzene to 2 for benzene or carbon tetrachloride. These results again refute the conclusions of Brown and Grayson on this problem.

The results obtained suggest that for other solvents also a characteristic and different dependence of the reaction rate on the aluminum chloride concentration will be found. Corresponding experiments for the reaction of tert. butyl chloride and cyclohexyl chloride with benzene (concentration of benzene 12.5 vol.-%, Table 4) actually showed that the order of reaction with respect to aluminum chloride in carbon disulfide solution is very close to 2, but for dichloroethane it is equal to 1.0-1.38, i.e., an intermediate value previously found for a mixed solvent comprising approximately equal parts of nitrobenzene and benzene or carbon tetrachloride.

Influence of solvents on the rate of alkylation. It follows from the data of Tables 2 and 3 that the reaction rate rises sharply with increasing content of nitrobenzene in its mixtures with carbon tetrachloride. For the purpose of more convenient representation of these results, we have taken the velocity constant of the reaction of tert. butyl chloride with benzene as unity for a nitrobenzene content of 12.5 vol.-%, an aluminum chloride concentration of 0.100 mole/liter, and a temperature of 20° (Table 6), and from the data of Tables 2 and 3 we calculated the relative velocities of this reaction for other compositions of the medium. It was necessary in this connection to convert the results of experiments with tert. amyl chloride, making use of the fact that its reactivity relative to tert. butyl chloride is equal to 0.31 on the basis of experiment 5 of Table 2 and experiment 2 of Table 3. The results are plotted in Fig. 2 which shows the sharp rise of reaction velocity with increasing content of nitrobenzene in the reaction mixture. Thus, a change of its concentration from 25 to 75 vol.-% causes the reaction rate to increase 85 times, i.e., even more sharply than for mixtures of benzene with nitrobenzene.

A comparison of the different substances as solvents for the alkylation reaction is made difficult by the necessity of the presence of nitrobenzene in the reaction mass (for homogenization of the solution) as well as of benzene (the latter in excess in relation to the halogen compound). Fig. 2 nevertheless shows that with a small quantity of nitrobenzene the rate of alkylation depends on its concentration to a small extent. The effect of addition of benzene is more marked, although only when strongly ionizing solvents are used (Fig. 3 of the preceding paper [1]).

Results of the appropriate experiments with the objective of determination of the relative "activities" of solvents in alkylations, and of the energies of activation are presented in Tables 5 and 6. In all of the experiments the initial concentration of halogen compound was 0.200 mole/liter and the benzene concentration was 12.5 vol.-% (except in the experiments where it was the main solvent).

The velocity constant of alkylation in different solvents, as a function of the temperature is plotted in Figure 3. This diagram shows that the experimental points fall fairly satisfactorily on the straight line of log velocity constant versus reciprocal temperature. The energy of activation in the different solvents was calculated from the slope of the straight-line plots (Table 7).

TABLE 4

| Solvent and temperature | Content of nitrobenzene (vol.-%) | Concentration of aluminum chloride (moles) | Number of parallel experiments | Velocity constant $\kappa_1$ (min$^{-1}$) | Reaction order with respect to $AlCl_3$ |
|---|---|---|---|---|---|
| | | tert.-Butyl chloride + benzene | | | |
| Carbon disulfide, 20° | 25.0 | 0.152 | 5 | 0.152 ± 3.1% | 2.09 |
| | 25.0 | 0.100 | 3 | 0.0635 ± 1.6% | |
| 1,1,2,2-Tetrachloroethane, 20° | 12.5 | 0.100 | 4 | 0.198 ± 2.3% | 1.6 |
| | 12.5 | 0.049 | 3 | 0.063 ± 0.5% | |
| 1,2-Dichloroethane, 10° | 12.5 | 0.049 | 4 | 0.250 ± 1.8% | 1.38 |
| | 12.5 | 0.025 | 3 | 0.099 ± 1.6% | |
| | | Cyclohexyl chloride + benzene | | | |
| 1,2-Dichloroethane, 40° | 11.0 | 0.100 | 6 | 0.0765 ± 1.0% | 1.0 |
| | 11.0 | 0.049 | 4 | 0.0375 ± 1.1% | |

TABLE 5

Reaction of Cyclohexyl Chloride with Benzene (Solvent: Dichloroethane, Concentration of Aluminum Chloride 0.100 Molar, Concentration of Nitrobenzene 11.0 vol.-%)

| Number | Temperature | Number of parallel experiments | Velocity constant $\kappa_1$ (min$^{-1}$) |
|---|---|---|---|
| 1 | 25.0° | 4 | 0.0165 ± 1.1% |
| 2 | 30.0 | 4 | 0.0285 ± 1.2% |
| 3 | 35.0 | 3 | 0.0475 ± 1.2% |
| 4 | 40.0 | 6 | 0.0765 ± 1.0% |

For comparative evaluation of the influence of the solvents on the rate of alkylation we assumed that the velocity constant of reaction of tert. butyl chloride with benzene in carbon tetrachloride solution at 20° (experiment 9, Table 6) was 1. Then from the tables and Fig. 2, also from the data of our preceding paper [1], we could calculate the relative velocities of reaction in other solvents. Due to the presence of benzene and nitrobenzene in the solution, a correction was introduced into the values obtained directly from Tables 5 and 6 in order to find the respective characteristic values for the pure solvents. The correction was found from Fig. 3 of our preceding paper [1], starting from the assumption that addition of nitrobenzene or benzene to the pure solvent has the same effect as their addition to a mixture of benzene and nitrobenzene of the same "activity" as the given solution. The relative "activities" of the solvents obtained in this fashion are shown in Table 7 together with the activation energies of the reactions and the dielectric constants of the solvents.

Comparison of the above results shows in particular the strong dependence of the rate of alkylation on the nature of the solvent, in complete contrast to the results of Brown and Grayson. This difference may be due, however, to some extent to the fact that our results were obtained with a low concentration of catalyst (0.100 molar), whereas Brown and Grayson worked with a concentration of aluminum chloride of up to 0.667 molar. The reaction rates in various solvents are therefore equalized owing to the change in the order of reaction with respect to aluminum chloride at higher concentrations of the latter.

Concerning the energies of activation, no definite relation between them and the nature of the solvent could be observed. In the case, for example, of the reaction of cyclohexyl chloride with benzene, the highest activation energy was found with active solvents, whereas in the reaction of tert. butyl chloride the opposite relation is observed. Only on comparing chemically similar solvents (chloro derivatives in this case) do we detect a slight lowering of the activation energy with increasing "activity" of the solvent. This change is insignificant, however, and it cannot account for the influence of the medium on the reaction rate. The nature of the solvent accordingly affects mainly the factor PZ of the rate equation.

## TABLE 6

Reaction of Tert. Butyl Chloride with Benzene

| No. | Concentration: nitrobenzene (vol. %) | Concentration: aluminum chloride (moles) | Temp. ± 0.05° | No. of parallel experiments | Velocity constant $k_1$ (min$^{-1}$) |
|---|---|---|---|---|---|
| | | Solvent: benzene | | | |
| 1 | 12.5 | 0.100 | 5.0° | 4 | 0.0390 ± 1.3% |
| 2 | 12.5 | 0.100 | 10.0 | 3 | 0.064 ± 1.2% |
| 3 | 12.5 | 0.100 | 15.0 | 4 | 0.107 ± 3.2% |
| 4 | 12.5 | 0.100 | 20.0 | 4 | 0.169 ± 2.3% |
| | | Solvent: carbon tetrachloride | | | |
| 5 | 25.0 | 0.203 | 10.0 | 4 | 0.0219 ± 1.9% |
| 6 | 25.0 | 0.203 | 15.0 | 3 | 0.0350 ± 1.0% |
| 7 | 25.0 | 0.203 | 20.0 | 4 | 0.054 ± 1.4% |
| 8 | 25.0 | 0.203 | 25.0 | 4 | 0.082 ± 1.1% |
| 9 | 12.5 | 0.100 | 20.0 | 4 | 0.0104 ± 2.9% |
| | | Solvent: carbon disulfide | | | |
| 10 | 12.5 | 0.100 | 10.0 | 4 | 0.0145 ± 2.4% |
| 11 | 12.5 | 0.100 | 15.0 | 3 | 0.0238 ± 1.6% |
| 12 | 12.5 | 0.100 | 20.0 | 4 | 0.0368 ± 2.1% |
| 13 | 12.5 | 0.100 | 25.0 | 3 | 0.0565 ± 1.7% |
| | | Solvent: 1,1,2,2-tetrachloroethane | | | |
| 14 | 12.5 | 0.100 | 5.0 | 4 | 0.049 ± 1.6% |
| 15 | 12.5 | 0.100 | 10.0 | 4 | 0.079 ± 1.2% |
| 16 | 12.5 | 0.100 | 15.0 | 3 | 0.121 ± 2.0% |
| 17 | 12.5 | 0.100 | 20.0 | 4 | 0.186 ± 2.7% |
| | | Solvent: 1,2-dichloroethane | | | |
| 18 | 12.5 | 0.025 | 5.0 | 3 | 0.0645 ± 1.4% |
| 19 | 12.5 | 0.025 | 10.0 | 4 | 0.099 ± 1.3% |
| 20 | 12.5 | 0.025 | 15.0 | 3 | 0.151 ± 1.4% |
| 21 | 12.5 | 0.025 | 20.0 | 4 | 0.218 ± 2.8% |

## TABLE 7

| Solvent | Dielectric constant | Relative activity | Energies of activation (kcal/mole): of reaction of cyclohexyl chloride with benzene | Energies of activation (kcal/mole): of reaction of tert. butyl chloride with benzene |
|---|---|---|---|---|
| Carbon tetrachloride | 2.24 | 1.0 | – | 14.9 ± 0.5 |
| Benzene | 2.28 | 2.5 | 17.5 ± 0.3 [1] | 15.5 ± 0.3 |
| Carbon disulfide | 2.64 | 4.0 | – | 15.1 ± 0.6 |
| 1,1,2,2-Tetrachloroethane | 8.0 | 30 | – | 14.4 ± 0.6 |
| 1,2-Dichloroethane | 10.5 | 170 | 18.9 ± 0.5 | 13.2 ± 0.7 |
| Nitrobenzene | 36.1 | 360 | 18.7 ± 0.8 [1] | – |

Comparison of the activity of solvents during alkylation with their dielectric constants throws some light on the mechanism of the influence of solvents. It is already evident from the data of the last table that the changes in these two parameters follow the same trend. A plot of the logarithm of the "activity" of the solvent against the reciprocal of the dielectric constant gives a straight line (Fig. 4) except in the case of tetrachloroethane for which the deviation is appreciable. A similar dependence was previously observed by Wynne-Jones [4] for the ionization constants of carboxylic acids. We are therefore forced to the conclusion that in our case the solubility influences the degree of ionization of one of the components of the reaction, namely the catalytic complex of aluminum chloride with nitrobenzene.

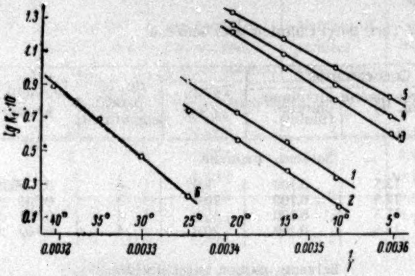


Fig. 3. Reaction velocity as a function of the temperature in the case of different solvents. For tert. butyl chloride: 1) carbon tetrachloride, 2) carbon disulfide, 3) benzene, 4) 1,1,2,2-tetrachloroethane, 5) 1,2-dichloroethane; for reaction with cyclohexyl chloride: 6) 1,2-dichloroethane.

## Evaluation of Results

The general kinetic equation of catalysis with the help of aluminum chloride that we derived in the preceding paper [1],

$$-\frac{dx}{dt}=\{k_{\mathrm{i}}[\mathrm{Al_2Cl_6}]^{0.5}+k_{\mathrm{m}}[\mathrm{Al_2Cl_6}]^{2}\}\,[\mathrm{RCl}]\,[\mathrm{ArH}]$$

is fully confirmed in the present investigation. The interplay of the ionic and the molecular mechanism of catalysis and the resulting variation in the orders of the reaction with respect to aluminum chloride are characteristic features of the action of this catalyst. Here the ionic catalysis is brought about by a cation and the molecular action by the undissociated molecule of the catalytic complex. For the interpretation of the mechanism of both types of catalysis, it is necessary to remember that simultaneous triple collisions between the reaction components occur very rarely. The reaction must therefore involve some bimolecular steps. For the ionic catalysis the first of these is interaction of the cation with the halogen compound which is an equilibrium step:

$$\mathrm{K^+ + RCl} \overset{K_h}{\rightleftarrows} \mathrm{K^+}\overset{\delta-}{\mathrm{Cl}} \longleftarrow \overset{\delta+}{\mathrm{R}}$$

In the resulting reaction complex the carbon-halogen bond is polarized to a sufficient extent for initiation of the subsequent reaction with benzene. We do not assume, however, that this bond is fully ruptured with formation of carbonium ions. Criticisms of these ideas were already noted in our previous papers [3], and they have recently been joined by those of some American authors [2, 6].

The second step of the reaction is bimolecular interaction of the reaction complex with the hydrocarbon, which we visualize (contrary to the theory of Brown and Grayson) as a true replacement of the hydrogen atom by its gradual displacement by the alkyl group which carries a partial positive charge:

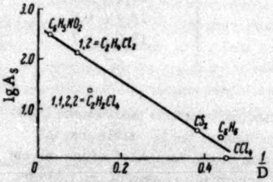


Fig. 4. Dependence of the "activity" of solvents on their dielectric constant.

$$K^{+}\overset{\delta-}{Cl} \leftarrow \overset{\delta+}{R} + ArH \leftrightarrows \left[K^{+}\overset{\delta-}{Cl}---\overset{\delta+}{R}---\overset{\delta-}{Ar}--\overset{\delta+}{H}\right] \xrightarrow{k_2'} K^{+} + HCl + ArR$$

Since the over-all rate of the process must be determined by the last reaction, we obtain the following kinetic equation:

$$-\frac{dx}{dt} = k_2'[K^{+}ClR][ArH] = k_2' \cdot K_h[K^{+}][RCl][ArH]$$

Bearing in mind that a cation is formed by dissociation of the catalytic complex [1]

$$[(C_6H_5NO_2)_2AlCl_2]\,[AlCl_4] \overset{K}{\rightleftarrows} [(C_6H_5NO_2)_2AlCl_2]^{+} + [AlCl_4]^{-} = K^{+} + A^{-},$$

we have at a low degree of dissociation:

$$[K^{+}] = \sqrt{K_k\,[Al_2Cl_6]}$$

Finally, we therefore obtain:

$$-\frac{dx}{dt} = k_2' \cdot K_k\sqrt{K_k}\,[Al_2Cl_6]^{0.5}\,[RCl]\,[ArH] = k_1\,[Al_2Cl_6]^{0.5}\,[RCl]\,[ArH],$$

which is also observed for the reaction in nitrobenzene solution, where $k_1$ is the velocity constant of the ionic catalytic process.

According to Moelwyn-Hughes [7] the velocity constant of a second-order reaction is determined by the number of collisions between activated molecules, the factor P of the rate equation being equal to unity, as he showed for a number of reactions. For the reaction of cyclohexyl chloride with benzene in nitrobenzene we then obtain:

$$k_2' = PZ \cdot e^{-\frac{E}{RT}} = 1 \cdot 2.8 \cdot 10^{11} \cdot e^{-\frac{18700}{R \cdot 303}} = 9 \cdot 10^{-3}\ \text{l/mole} \cdot \text{sec} = 0.53\ \text{l/mole} \cdot \text{min}$$

The following velocity constant was found [1] experimentally for this reaction with an aluminum chloride concentration of 0.1 molar:

$$k_2 = \frac{k_1}{[C_6H_6]} = \frac{0.047}{1.408} = 0.0334\ \text{l/mole} \cdot \text{min}$$

From this we obtain:

$$k_2'K_h\sqrt{K_k}\,[Al_2Cl_6]^{0.5}\,[RCl]\,[ArH] = k_2\,[RCl]\,[ArH]$$

and

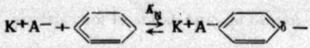
$$K_h\sqrt{K_k} = \frac{k_2}{k_2'\,[Al_2Cl_6]^{0.5}} = \frac{0.0334}{0.53\,(0.05)^{0.5}} = 0.28.$$

Since it was previously shown [8] that the reactivity both of halogen derivatives and aromatic compounds depends only on the changes in the activation energies of these reactions, the structure of the organic compounds only influences the factor $e^{-E/RT}$ which governs the number of effective collisions. On the other hand, solvents with a weak action (as shown above) on the activation energy, manifest their action by a change of the magnitude of $K_h\sqrt{K_k}$ and in particular of the equilibrium constant during dissociation of the catalytic complex $K_k$. This effect also determines the dependence of the influence of solvents on their dielectric constant.* Consequently, the value of $K_h\sqrt{K_k} = 0.28$ must be constant for a given composition of medium and independent of the structure of the reacting organic compounds.

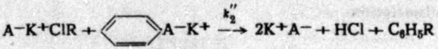
In the case of molecular catalysis, which predominates in weakly dissociated solvents, the halogen compound is activated by the undissociated molecule of the catalytic complex:

$$K^+A^- + RCl \overset{K'_{\text{h}}}{\rightleftarrows} A^-K^+\overset{\delta-}{Cl} \leftarrow \overset{\delta+}{R}$$

Due, however, to the lower strength of its electric field (relative to that created by the ion) the polarization of the carbon-halogen bond proves to be insufficient for direct reaction with benzene. The latter must also be activated by a second molecule of the dipole:



The rate-determining process is the bimolecular interaction of the resulting complexes:



In this event we obtain the kinetic equation:

$$-\frac{dx}{dt} = k''_2\,[K^+A^-RCl]\,[K^+A^-C_6H_6] = k''_2K'_{\text{h}}[KA][RCl]\cdot K_{\text{u}}[KA][C_6H_6] =$$

$$= k''_2\cdot K'_{\text{h}}\cdot K_{\text{u}}[Al_2Cl_6]^2[RCl][ArH] = k_{\text{m}}[Al_2Cl_6]^2[RCl][ArH],$$

which is also observed for reaction in weakly ionized solvents; where $k_{\text{m}}$ is the rate constant of the molecular catalytic reaction.

Previously we found $k_2$ = 0.0074 liter/mole. min. and E = 14.7 kcal/ mole for the reaction of tert. butyl chloride with benzene in carbon tetrachloride solution at 20° and a concentration of 0.1 molar $AlCl_3$. Hence, by a similar procedure we obtain:

$$k''_2 = 2.8\cdot 10^{11}\cdot e^{-\frac{14700}{R\cdot 293}} = 3.5\ \text{l/mol. sec} = 210\ \text{l/mol. min}$$

$$K'_{\text{h}}\cdot K_{\text{u}} = \frac{k_2}{k''_2\,[Al_2Cl_6]^2} = \frac{0.074}{210\,(0.05)^2} = 0.014.$$

This value is considerably lower than that for the ionic reaction. Molecular catalysis is therefore slower than ionic catalysis, mainly due to the considerable decrease in the equilibrium constants during formation of reaction complexes, in particular unstable complexes with hydrocarbons.

Our proposed mechanism of alkylation in presence of aluminum chloride is not limited to solutions containing nitrobenzene. This catalyst is known to give complex compounds with many organic compounds all of which carry the electric current [9]. Their formation may be a critical factor in the acceleration of a reaction, due to catalysis by the cation of these complexes, and this would also explain the high activity of Gustavson complexes (the lower layers formed during the alkylation) which are likewise ionized compounds [10].. Conversely, the poor activity of solid aluminum chloride is determined by its molecular crystalline lattice and the resulting slow molecular catalysis, which changes into the rapid ionic process as the Gustavson complexes are gradually formed.

Walker [11] also attempted to correlate the catalytic activity of aluminum chloride with ionization; he did not realize, however, that a part is here played not only by the electrical conductivity but also by the structure of the positively charged ion which depends on the structure of the organic component; the latter determines the catalytic activity of the ion itself. We know, for instance, that in complexes with ketones the catalyst is completely deactivated in spite of the ionization.

The dual mechanism of catalysis during alkylation in presence of aluminum chloride has an interesting analogy in the characteristics of catalytic action of acids in many organic reactions [12]. Thus, the fractional order of the reaction with respect to aluminum chloride, corresponding to the law of dilution of weak electrolytes, has a parallel in the case of catalysis with the hydrogen ion [13]. The kinetic equation that we derived, in which the catalytic coefficient consists of two components, corresponds to an analogous equation for acid catalysis [14] in which not only the hydrogen ion but also the undissociated molecule of acid is catalytically active. In this respect our data are consistent with the dualistic theory of acid catalysis, so that we can regard reactions in presence of aluminum chloride as one case of general acid catalysis. This interpretation is supported by the fact that suitable catalysts for alkylation reactions are not only electron acceptors of the type of metallic halides, but also a whole series of mineral acids.

## SUMMARY

1. It was confirmed that the order of the alkylation of aromatic compounds with halogen-containing compounds with respect to aluminum chloride varies in dependence on the type of solvents; the latter also have a marked influence on the reaction rate. The data of Brown and Grayson on this problem are refuted.

2. The theory of the ionic and molecular mechanisms of aluminum chloride-catalyzed reactions is further developed.

## LITERATURE CITED

[1] N. N. Lebedev, J. Gen. Chem. 24, 664 (1954).*

[2] H. C. Brown, M. Grayson, J. Am. Chem. Soc. 75, 6285 (1953).

[3] R. P. Bell, J. Chem. Soc. 1931, 1371.

[4] W. F. K. Wynne-Jones, Proc. Roy. Soc. A 140, 440 (1933).

[5] N. N. Lebedev, Communications on the Scientific Works of Members of the All-Union Mendeleev Chemical Society No. 2, 31 (1947); J. Phys. Chem. 22, 1505 (1948); V. V. Korshak and N. N. Lebedev, Proc. Acad. Sci. USSR 57, 263 (1947); J. Gen. Chem. 18, 1766 (1948).

[6] H. C. Brown, H. W. Pearsall, L. P. Eddy, W. J. Wallace, M. Grayson, K. LeRoy Nelson, Ind. Eng. Chem. 45, 1462 (1953).

[7] E. A. Moelwyn-Hughes, Kinetics of Reactions in Solutions [Russian translation] (State United Sci. Tech. Press 1938).

[8] N. N. Lebedev, Trans. Moscow Mendeleev Inst. Chem. Tech. 23, 40 (1956).

[9] C. Thomas, Anhydrous Aluminum Chloride in Organic Chemistry [Russian translation] (For. Lit. Press 1949).

[10] V. Neminskii and V. Plotnikov, J. Russ. Chem. Soc. 40, 391 (1908); V. Plotnikov, J. Russ. Chem. Soc. 40, 1247 (1908).

[11] J. W. Walker, J. Chem. Soc. 85, 1082 (1904).

[12] G. M. Schwab, Catalysis from the Standpoint of Chemical Kinetics [Russian translation] (United Sci. Tech. Press 1934).

[13] H. Goldschmidt, E. Sunde, Ber. 39, 711 (1906), H. Braune, Z. Phys. Ch. 85, 170 (1913).

[14] H. S. Snethlage, Z. Phys. Ch. 85, 211 (1913); Z. Elektroch. 18, 539 (1912).

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*Original Russian pagination. See C. B. Translation.

# STEREOCHEMICAL INVESTIGATIONS

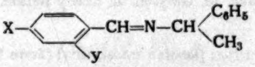
## III. SCHIFF BASES FROM OPTICALLY ACTIVE α-PHENYLETHYLAMINE

A. P. Terent'ev and V. M. Potapov

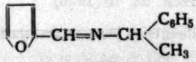
The literature contains relatively little information about optically active Schiff bases. Betti [1] described a series of such substances derived from (+)-α-(β-naphthol)-benzylamine. He had previously obtained several products of condensation of optically active α-(p-anisyl)-ethylamine with substituted benzaldehydes [2]. Several Schiff bases from isomeric methylamines [3, 4] and fenchylamine [4, 5] have also been described.

In the course of an investigation of derivatives of optically active α-phenylethylamine, we prepared a series of Schiff bases (I-XVI) from this amine.

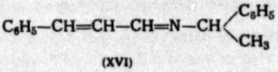
Data for these bases are given in the table. After this work had been completed and the results prepared for publication, a paper was published by Nerdel and others [6] which described several Schiff bases from (−)-α-phenylethylamine, including 4 of our preparations (II, V, VII, XI). Nerdel measured the optical activity in benzene, alcohol, chloroform and dioxane, whereas we performed the measurements in benzene, methanol, acetone and dichloroethane. Consequently, the data overlap only for the benzene solutions (the agreement was generally good); in other respects the two papers supplement one another.



(I—XI); (XIII—XV)



(XII)

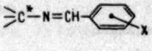


(XVI)

| № | X | y |
|---|---|---|
| (I) | $AsO_3H_2$ | H |
| (II) | H | H |
| (III) | iso -$C_3H_7$ | H |
| (IV) | $CH_3$ | H |
| (V) | $OCH_3$ | H |
| (VI) | $NO_2$ | H |
| (VII) | Cl | H |
| (VIII) | Br | H |
| (IX) | $NH_2$ | H |
| (X) | $-OCH_2O-$ | H |
| (XI) | $N(CH_3)_2$ | H |
| (XIII) | H | $OCH_3$ |
| (XIV) | H | OH |
| (XV) | H | $NO_2$ |

Examination of the table reveals a considerable divergence between the experimental and calculated values of molecular refraction; this, however, is not unexpected, since according to Auwers [7] the exaltation of molecular refraction of benzylideneamines may be as much as four units.

The tabulated data for optical activity are of particular interest for the evaluation of the influence of the nature of the substituent in the aromatic ring on the magnitude of the optical rotation in a system of the type of



Schiff Bases from (+)-α-Phenylethylamine

| Substance number | Temperature |  | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ |  | Yield % | Empirical formula | Found % |  |  | Calculated % |  |  | Molecular rotation in solvents |  |  |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  | of melting | of boiling (pressure in mm) |  |  | found | calc. |  |  | C | H | N | C | H | N | benzene | methanol | acetone | dichloroethane |
| (I) | 79° | — | — | — | — | — | 96 | $C_{15}H_{16}O_3NAs$ | — | — | 4.22 | — | — | 4.21 | — | −83° | — | — |
| (II) | — | 161−163° (9) | 1.025 | 1.5888 | 68.8 | 67.3 | 92 | $C_{15}H_{15}N$ | 86.07 | 7.18 | 6.79 | 86.12 | 7.23 | 6.69 | −168° | −160 | −188° | −154° |
| (III) | 22 | 194−196 (7) | 0.9825 | 1.5621 | 83.0 | 81.1 | 88 | $C_{18}H_{21}N$ | — | — | 5.28 | — | — | 5.36 | −184 | −146 | −184 | −164 |
| (IV) | 91−93 | — | — | — | — | — | 94 | $C_{16}H_{17}N$ | — | — | 6.31 | — | — | 6.28 | −234 | −179 | −229 | −189 |
| (V) | — | 198 (6) | 1.0635 | 1.5973 | 76.7 | 73.5 | 58 | $C_{16}H_{17}ON$ | — | — | 5.76 | — | — | 5.85 | −248 | −219 | −263 | −220 |
| (VI) | Oil |  | — | — | — | — | — | — | — | — | — | — | — | — | −271 | −223 | −254 | −221 |
| (VII) | 76 | — | — | — | — | — | 93 | $C_{15}H_{14}NCl$ | 73.42 | 5.79 | — | 73.96 | 5.79 | — | −258 | −190 | −200 | −182 |
| (VIII) | 89−90 | — | — | — | — | — | 78 | $C_{15}H_{14}NBr$ | — | — | 5.08 | — | — | 4.85 | −270 | −235 | −271 | −217 |
| (IX) | 95−97 | — | — | — | — | — | 81 | — | — | — | — | — | — | — | −314 | −330 | −390 | −294 |
| (X) | — | 198−200 (4) | 1.1495 | 1.5940 | 74.7 | 74.1 | 87 | $C_{16}H_{15}O_2N$ | — | — | 5.32 | — | — | 5.51 | −375 | −327 | −371 | −336 |
| (XI) | 84 | — | — | — | — | — | 74 | $C_{17}H_{20}N_2$ | — | — | 11.11 | — | — | 11.10 | −460 | −463 | −457 | −436 |
| (XII) | — | 151−154 (9) | 1.0681 | 1.5788 | 62.0 | 61.6 | 85 | $C_{13}H_{13}ON$ | — | — | 6.73 | — | — | 7.03 | −132 | −200 | −216 | −168 |
| (XIII) | 101 | 178−181 (4) | 1.0573 | 1.5894 | 76.3 | 73.5 | 62 | $C_{16}H_{17}ON$ | — | — | 5.80 | — | — | 5.85 | + 85 | + 74 | + 16 | + 17 |
| (XIV) | 76 | — | — | — | — | — | 84 | $C_{15}H_{15}ON$ | 79.30 | 6.89 | 6.75 | 79.64 | 7.13 | 6.19 | −402 | −433 | −330 | −341 |
| (XV) | — | 168−169 (2) | 1.1651 | 1.5970 | 74.4 | 72.3 | 83 | — | — | — | — | — | — | — | +227 | +129 | + 59 | +106 |
| (XVI) | 22 | — | — | — | — | — | — | — | — | — | — | — | — | — | − 23 | + 13 | − 38 | + 6 |

The first point that is raised by the data in the table is as follows: whereas Betti had started from α-(β-naphthol)-benzylamine and obtained Schiff bases with a sign of rotation identical with that of the original amine, in the case of Schiff bases from α-phenylethylamine their sign of rotation is opposite that of the original amine. Moreover, the data in the table do not reveal the dependence on the "electronegative" or "electropositive" character of the substituent that Betti inferred from his measurements. In our case, benzaldehyde with any substituent in the para-position to the aldehyde group gives a Schiff base whose molecular rotation is higher than that of the product of condensation with unsubstituted benzaldehyde. This forces us to the conclusion that the action of the substituent on the magnitude of rotation cannot be explained solely as an electronic effect. This conclusion is strengthened on consideration of the data obtained for compounds of the ortho-series. If the sole decisive factor had been the electronic influence of the substituent transmitted along the conjugated chain to the asymmetric center, then the magnitude of the rotation for compounds containing a substituent in the ortho-position should not appreciably differ from the rotation of the analogous para-compounds. Furthermore, experimental data reveal the characteristic behavior of compounds of the ortho-series. Whereas all of the compounds of the para-series are characterized by a high molecular rotation whose sign is opposite to that of the original amine, the sign of the rotation of the original amine is retained in the case of ortho-methoxy (XIII) and ortho-nitro (XV) derivatives on transition to the corresponding Schiff base. These two compounds are distinguished by a high dependence of the magnitude of rotation on the solvent. The same is true of the Schiff bases from furfural and cinnamaldehyde.

An insight into the causes of the unusual behavior of ortho-substituted derivatives may be obtained by using models to examine the possibility of free rotation round the single bonds present in the system*. Such considerations indicate the possibility of formation by ortho-compounds of preferred configurations (rotational isomers) due to steric hindrance round the bond between the substituted benzene ring and the -CH=N- group. Since the formation of a hydrogen bond -O-H ····N is very probable for salicylal-α-phenylethylamine (XIV), the preferred configuration in this case must probably be

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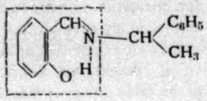
* In another paper [8] we considered the role of rotational isomerism with reference to the literature and to our own experiments.



Here the whole of the group enclosed in the dashed frame must be visualized as fixed in the plane of the diagram.

In the case of the ortho-methoxy derivative, for which the formation of a similar hydrogen bond is impossible and in which at the same time the bulkier $OCH_3$ group opposes the formation of a "plane" rotational isomer, the "nonplanar" configurations are precisely the ones that will be preferred. This also applies to the ortho-nitro- derivative, and thus accounts for the considerable difference between the optical rotations of these two Schiff bases in comparison with the salicylal derivative.

It is also evident that the nature of the solvent will have a profound effect on the stability of one or the other of the rotational isomers resulting from intramolecular interaction of the groups. This provides an explanation of the great dependence of the magnitude of rotation on solvents which is observed for compounds (XIII) and (XV) (for obvious reasons this does not apply to the "fixed" hydrogen bond of the salicylal derivative). Similarly we account for the analogous strong dependence in the case of (XII), since the α-furyl residue is also a characteristic "nucleus with an ortho-substituent". A similar explanation may also be offered for Nerdel's observation [6] of the great dependence of $[\alpha]_D$ on the solvents in the case of naphthal-α-phenylethylamine and the Schiff base from the same amine and pyridine-3-aldehyde.

## EXPERIMENTAL

α-Phenylethylamine was prepared by reductive amination of acetophenone by the Leuckart method [9]. It was resolved into the optical antipodes with acid borneol sulfate [10] or tartaric acid in methanol [11]. Successive employment of both methods affords the possibility of convenient preparation of the dextro- as well as the levoratatory amine.

Racemic benzal-α-phenylethylamine. To 21.2 g of freshly distilled benzaldehyde was gradually added a solution of 24.2 g of DL-α-phenylethylamine in 60 ml of benzene, and the mixture was refluxed for an hour. The benzene and the water of reaction were then distilled off, and the residue was distilled in vacuo. Yield 27 g (65%).

B. p. 161-163° (9 mm), $d^{20}_4$ 1.025, $n^{20}D$ 1,5888, $MR_D$ 68.79; calculated 67.27.

Kann and Tafel [12] also prepared this substance and report b. p. 273-275° (14 mm); they did not give other constants. The erroneous boiling point was also entered in Beilstein [13].

Benzal-(+)-α-phenylethylamine (II). The procedure was the same as for the preceding preparation, starting from benzaldehyde and (+)-α-phenylethylamine in 35 ml of methanol. Constants for this and other Schiff bases from optically active α-phenylethylamine and data for their molecular rotation appear in the table. In the case of other substances we shall report only the values found for specific rotations which serve as a basis for the calculation of the magnitude of $[M]_D$.

$[\alpha]^{18}D$ −83.2° (without solvent, $l$ 1.0); −80.3° (benzene, c 7.7); −76.6° (methanol, c 5.0); −90.1° (acetone, c 4.3); −73.4° (dichloroethane, c 4.1).

p-Isopropylbenzal-(+)-α-phenylethylamine (III). Prepared on the same lines as the preceding compound from (+)-α-phenylethylamine and freshly distilled cuminal without a solvent.

$[\alpha]^{20}D$ −73.2° (benzene, c 10.0); −58.3° (methanol, c 7.2); −73.1° (acetone, c 5.3); −65.5° (dichloroethane, c 3.5).

p-Methoxybenzal-(+)-α-phenylethylamine (V). Prepared as above from (+)-α-phenylethylamine and freshly distilled anisaldehyde.

$[\alpha]^{20}D$ −103.5° (benzene, c 8.0); −91.5° (methanol, c 5.1); −109.8° (acetone, c 5.0); −93.4° (dichloroethane, c 3.8).

Piperonal-(+)-α-phenylethylamine (X). Prepared as above from (+)-α-phenylethylamine and piperonal.

$[\alpha]^{20}D$ −148.4° (benzene, c 7.5); −129.0° (methanol, c 4.5); −146.2° (acetone, c 4.8); −132.5° (dichloroethane, c 2.2).

Furfural-(+)-α-phenylethylamine (XII). Prepared from equivalent quantities of (+)-α-phenylethylamine and freshly distilled furfural. Condensation was effected by 4-days' standing at room temperature. The constants of the prepared compound are identical with those reported in the paper by Nerdel and others, but our value for the optical activity was considerably higher than that of the authors cited.

$[\alpha]^{20}_{D}$ −96.0° (without solvent, *l* 1.0); −66.1° (benzene, c 6.4); −100.6° (methanol, c 4.8); −108.3° (acetone, c 5.9); −84.2° (dichloroethane, c 2.5).

o-Methoxybenzal-(+)-α-phenylethylamine (XIII). Prepared from equimolar quantities of (+)-α-phenylethylamine (not completely resolved − optical purity 59.5%) and o-methoxybenzaldehyde by condensation on prolonged standing at room temperature. A parallel experiment was run with α-phenylethylamine of 100% optical purity; the reaction product was not distilled; the water was removed by aspiration in vacuo on a water bath and the oily residue was used directly for the polarimetric measurements. The agreement between the two sets of results showed that the use of the amine in a state of incomplete optical purity was permissible and that the undistilled product of condensation could be used for exploratory determinations of $[\alpha]_D$ (error of the order of ± 0.5°).

$[\alpha]^{20}_{D}$ +79.3° (benzene, c 10.0); +70.0° (methanol, c 3.6); +15.4° (acetone, c 3.3); +15.8° (dichloroethane, c 2.5)*.

o-Nitrobenzal-(−)-α-phenylethylamine (XV). Prepared by condensation of equimolecular quantities of (−)-α-phenylethylamine** and o-nitrobenzaldehyde.

$[\alpha]^{20}_{D}$ −78.2° (without solvent, *l* 1.0); −89.5° (benzene, c 7.5); −60.9° (methanol, c 3.5); −23.1° (acetone c 4.7); −41.4° (dichloroethane, c 1.7).

Schiff base from (−)-α-phenylethylamine and cinnamaldehyde (XVI). A mixture of equimolecular quantities of freshly distilled cinnamaldehyde and (−)-α-phenylethylamine was left for 1 hour on a warm water bath; the water of reaction was removed by aspiration in vacuo; the residue crystallized on standing in a refrigerator. Due to the low melting point (about 22°), the crystals could not be purified by recrystallization. Determinations were therefore carried out on a product washed with the minimum quantity of ether and dried in vacuo.

$[\alpha]^{20}_{D}$ −26.3°(without solvent, *l* 1.0); 9.7° (benzene, c 3.0); −5.3° (methanol, c 3.3); 16.1° (acetone, c 1.8); −2.7° (dichloroethane, c 1.2).

Salicylal-(−)-α-phenylethylamine (XIV). A mixture of 12.23 g of freshly distilled salicylaldehyde and 13.0 ml of (−)-α-phenylethylamine in 20 ml of methanol was heated for 30 minutes on a water bath; a picric-yellow precipitate came down on cooling and was recrystallized from methanol. Yield 19.0 g (84%).

$[\alpha]^{20}_{D}$ +202° (methanol, c 2.1); +187° (benzene, c 2.2); +147° (acetone, c 2.7); +151° (dichloroethane, c 1.5).

p-Dimethylaminobenzal-(−)-α-phenylethylamine (XI). This was prepared on the same lines as the preceding compound, starting from (−)-α-phenylethylamine and p-dimethylaminobenzaldehyde.

$[\alpha]^{20}_{D}$ +182.5° (benzene, c 7.4); +183.4° (methanol, c 3.6); +181.4° (acetone, c 6.3); +172.8° (dichloroethane, c 2.4).

p-Aminobenzal-(−)-α-phenylethylamine (IX). Prepared from (−)-α-phenylethylamine and p-aminobenzaldehyde by the same procedure.

$[\alpha]^{20}_{D}$ +140.2° (benzene, c 3.8); +143.8° (methanol, c 4.2); +174.0 (acetone, c 3.4); +131.1° (dichloroethane, c 2.0).

p-Chlorobenzal-(−)-α-phenylethylamine (VII). Prepared from (−)-α-phenylethylamine and p-chlorobenzaldehyde as above.

$[\alpha]^{20}_{D}$ +106° (benzene, c 2.4); +77.5° (methanol, c 2.0); +81.8° (acetone, c 1.8); +74.6° (dichloroethane, c 1.0).

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* All values of $[\alpha]_D$ recalculated for optically pure product.

** The experimental values are given with the opposite sign in the table in all cases when (−)-α-phenylethylamine was used.

p-Bromobenzal-(−)-α-phenylethylamine (VIII). Prepared analogously to the preceding compound from (−)-α-phenylethylamine and p-bromobenzaldehyde.

$[\alpha]^{20}D$ +93.5° (benzene, c 1.9); +81.6° (methanol, c 2.0); +94.0° (acetone, c 2.4); +75.7° (dichloroethane, c 1.7).

p-Tolyl -(+)-α-phenylethylamine (IV). Prepared analogously to the preceding compound from (+)-α-phenylethylamine and p-tolylaldehyde.

$[\alpha]^{20}D$ −104.8° (benzene, c 6.1); −80.2° (methanol, c 4.2); −102.6° (acetone, c 4.2); −84.8° (dichloroethane, c 3.1).

p-Arsinacidobenzal-(−)-α-phenylethylamine (I). Prepared from (−)-α-phenylethylamine and benzaldehyde-p-arsinic acid on the same lines as the previous preparation.

$[\alpha]^{20}D$ +24.8° (methanol, c 3.1); −1.5° (water, c 2.9); +39.7° (0.7% aqueous NaOH solution). No determinations of $[\alpha]_D$ were made in the other solvents due to the poor solubility of the substance.

p-Nitrobenzal-(−)-α-phenylethylamine (VI). Prepared by condensation of (−)-α-phenylethylamine with p-nitrobenzaldehyde on a water bath; water of reaction was removed by aspiration in vacuo. Rotations were measured on the undistilled condensation product.

$[\alpha]^{20}D$ +106.4° (benzene, c 6.2); +88.3° (methanol, c 4.2); +100.0° (acetone, c 4.0); +87.0° (dichloroethane, c 1.8).

## SUMMARY

1. Schiff bases were prepared from optically active α-phenylethylamine and benzaldehyde, 13 substituted benzaldehydes, cinnamaldehyde and furfural.

2. Optical activities of the prepared Schiff bases were determined in benzene, methanol, acetone and dichloroethane.

3. The results are utilized for clarification of the problem of the possible influence of rotatory isomerism on the magnitude of the rotation.

## LITERATURE CITED

[1] M. Betti, Trans. Far. Soc. 26, 337 (1930).

[2] M. Betti, A. Capaccioli, Gazz. 50, II, 276 (1920).

[3] J. Read, Trans. Far. Soc. 26, 441 (1930).

[4] A. Binz, Z. Phys. Ch. 12, 723 (1893).

[5] O. Wallach, A. Binz, Lieb. Ann. 275, 315 (1893).

[6] F. Nerdel, K. Becker, G. Kresze, Ber. 89, 2862 (1956).

[7] K. v. Auwers, B. Ottens, Ber. 57, 456 (1924).

[8] V. M. Potapov and A. P. Terent'ev, Vestnik Moscow State Univ., Math., Mech., Astron., Phys. and Chem. Series No. 5, 179 (1957).

[9] Synth. Org. Prep. Vol. 2, 526 (1949) [Russian translation].

[10] A. P. Terent'ev and V. M. Potapov, J. Gen. Chem. 26, 1225 (1956).*

[11] W. Theilacker, H. G. Winkler, Ber. 87, 690 (1954).

[12] M. Kann, J. Tafel, Ber. 27, 2306 (1894).

[13] Beilst. XII, 1095 (1929).

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# PREPARATION OF α-AMINOACIDS VIA FURAN DERIVATIVES

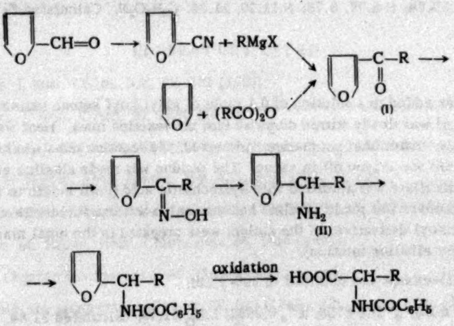
A. P. Terent'ev and R. A. Gracheva

With the aim of verifying the structure of 2-methyl-1-furylcyclopropane that he had prepared, N. M. Kizhner [1] subjected it to oxidation with potassium permanganate. In this way the furan ring was converted into carboxyl, a yield of up to 77% of 2-methylcyclopropanecarboxylic acid being obtained. V. F. Kucherov [2] performed a similar oxidation to verify the structure of butyl and isobutyl furyl carbinols (in the form of ethyl ethers).

The facility of transformation of the furan ring into carboxyl indicated the possibility of utilizing this reaction for the synthesis of derivatives of carboxylic acids.

Furfural and furan are not only readily accessible, but can be used as starting substances for diverse derivatives. Many syntheses of furylketones from furan have been described on the basis of reactions of the Friedel-Crafts type with acid chlorides and anhydrides. Furfural easily gives 2-furoic acid, or (via the oxime) 2-furonitrile. The latter can be transformed into various ketones by reaction with organomagnesium compounds. On this basis, we decided to exploit the reactivity of furans for synthesis of α-aminoacids containing the furan ring as the potential carboxyl.

The following reaction schemes are involved:



It should be noted that the amines serving as intermediates in this sequence of reactions are themselves of definite interest; only a few representatives of this group have been studied.

We applied the above-described transformations to three compounds (R = $CH_3$, $C_3H_7$, n-$C_4H_9$). Acetylfuran was prepared from furan and acetic anhydride in presence of phosphoric acid [3]; propyl and butyl furyl ketones were prepared from 2-furonitrile by the Grignard reaction [4]. Yields of ketones 60-70%. Reduction of the oximes of the ketones to the corresponding amines with zinc and acetic acid gives yields of 50-60%. Oxidation of the benzoyl derivatives of the amines was effected with potassium permanganate in an alkaline medium. In this fashion we obtained the benzoyl derivatives of three aminoacids – alanine, norvaline and norleucine – in yields of 50-70%.

## EXPERIMENTAL

### Alkyl-α-Furyl Ketones (I)

n-Butyl and propyl furyl ketones. Furonitrile (0.4 mole) in absolute ether was added (with stirring and cooling) to the Grignard reagent prepared from 0.5 mole alkyl bromide and 0.5 mole magnesium in absolute ether. The reaction mass was left overnight and then decomposed with 10% hydrochloric acid. The ketone was extracted with ether and dried. After the solvent had been driven off, the ketone was distilled in vacuo.

For preparation of the oxime, the ketone (0.1 mole) was dissolved in 50 ml of 95% alcohol and mixed with an aqueous solution of 0.2 mole of hydroxylamine hydrochloride and 0.2 mole of potassium carbonate. The mixture was boiled for 3 hours on an oil bath. After cooling, the alcohol was distilled off in vacuo and the oxime was extracted with ether.

n-Butyl furyl ketone. Yield 60%. B. p. 100-101° (10 mm), $n_D$*1.4929.

Oxime. Yield 85%, b. p. 131-132° (10 mm).

Found %: N 8.03. $C_9H_{13}O_2N$. Calculated %: N 8.38.

Propyl furyl ketone. Yield 60%, b. p. 96° (20 mm), $n^{16}D$ 1.4992.

Oxime. Yield 90%, b. p. 119° (10 mm).

Found %: C 62.58, 62.47; H 7.43, 7.28. $C_8H_{11}O_2N$. Calculated %: C 62.72; H 7.23.

Acetylfuran was prepared by heating 1 mole of furan, 2 moles of acetic anhydride and 20 g of phosphoric acid on a water bath at 60-70° for 2 hours. After cooling, the reaction mass was decomposed with water and neutralized with sodium carbonate. The ketone was extracted with ether. Yield of acetylfuran 70%, b. p. 74° (22 mm) [3], b. p. 66-68° (11-12 mm) [3].

Acetylfuran oxime was prepared as described above. After the ether had been driven off, the oxime was filtered. Yield 90%, m. p. 94-95°.

Found %: C 57.55, 57.74; H 5.77, 5.73; N 11.29, 11.35. $C_6H_7O_2N$. Calculated %: C 57.59; H 5.64; N 11.19.

### Amines (II)

25 g of zinc dust was added to a solution of 0.1 mole of alkyl furyl ketone oxime in 100 ml of methyl alcohol. Acetic acid (50 g) was slowly stirred dropwise into the reaction mass. Heat was developed and the mixture turned light yellow. After heat generation had ceased, the reaction mass was heated for 3 hours on a water bath. The acetic acid was driven off in vacuo. The residue was made alkaline and the amine was distilled off in steam. The distillate was acidified with hydrochloric acid (until acidic to Congo) and evaporated to a small volume. The product was made alkaline and the amine was extracted with ether and dried with caustic alkali. The N-benzoyl derivatives of the amines were prepared in the usual manner (treatment with benzoyl chloride in strongly alkaline solution).

1-Amino-1-(α-furyl)-ethane was obtained in 50% yield.

B. p. 145-147° (740 mm), $n^{20}D$ 1.4758, $d^{20}_4$ 0.9856, $MR_D$ 31.79; calculated 31.84.

Literature data [5]: b. p. 155°(752 mm), $n^{21}D$ 1.4799, $d^{20}_4$ 1.008.

The benzoyl derivative had m. p. 89-90° (from acetone); yield 96%.

Found %: C 72.16, 72.34; H 6.18, 6.10; N 6.64, 6.59. $C_{13}H_{13}O_2N$. Calculated %: C 72.55; H 6.08; N 6.55.

1-Amino-1-(α-furyl)-butane was obtained in 60% yield.

B. p. 92° (20mm), $n^{20}D$ 1.4735, $d^{20}_4$ 0.9583, $MR_D$ 40.88; calculated 41.07.

Literature data [6]: b. p. 83-85° (14 mm).

The benzoyl derivative was obtained in 90% yield; m. p. 80°.

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* As in original — Publisher's note.

1-Amino-1-(α-furyl)-pentane was obtained in 60% yield.

B. p. 104° (24 mm), $n^{20}D$ 1.4726, $d^{20}_4$ 0.9494, $MR_D$ 45.28; calculated 45.69.

Found %: C 70.93, 71.03; H 9.69, 9.88. $C_9H_{15}ON$. Calculated %: C 70.55; H 9.87.

The benzoyl derivative was obtained in 95% yield; m. p. 72° (from ligroine).

Found %: N 5.17, 5.09. $C_{16}H_{19}O_2N$. Calculated %: N 5.44.

### Benzoyl Derivatives of α-Aminoacids

To a solution of 0.01 mole of benzoyl derivative of amine in 100 ml of acetone was added 1 ml of 20% potassium hydroxide, and a solution of 8.2 g of potassium permanganate in 250 ml of water was stirred in (temperature of reaction mixture not higher than 15°). After decolorization of the mass, a further 8.3 g of finely pulverized potassium permanganate was added and the mixture left overnight. The manganese dioxide was filtered off and washed with hot water; the combined filtrates were evaporated to a volume of 25 ml. Hydrogen chloride was passed into the solution; the precipitated benzoyl derivative of the aminoacid was recrystallized from water or dilute alcohol.

Benzoylalanine. Yield 50%, m. p. 163-164° (from water) [7].

Found %: N 7.23, 7.10. $C_{10}H_{11}O_3N$. Calculated %: N 7.25.

Benzoylnorvaline. Yield 60%, m. p. 151-152° [8].

Found %: N 6.14, 6.28. $C_{12}H_{15}O_3N$. Calculated %: N 6.33.

Benzoylnorleucine. Yield 70%: m. p. 131-132° (from aqueous alcohol) [9].

Found %: N 5.78, 6.07. $C_{13}H_{17}O_3N$. Calculated %: N 5.95.

## SUMMARY

A method was developed for the preparation of α-aminoacids (benzoyl derivatives) which involved the following steps: α-furylketones, oximes, amines, benzoylamines, oxidation of the latter to N-benzoyl-α-aminoacids.

## LITERATURE CITED

[1] N. M. Kizhner, J. Russ. Chem. Soc. 61, 781 (1929).

[2] V. F. Kucherov, J. Gen. Chem. 20, 1889 (1950).*

[3] W. Gruber, Canad. J. Chem. 31, 564 (1953); Russ. Jour. Chem. 16306 (1954).

[4] J. Asahina, J. Murayma, Arch. Pharm. 252, 435; Zbl. 1914, II, 1916.

[5] J. Asahina, A. Fujita, J. Pharm. Soc. Japan 490, 1084 (1922); 17, 2578 (1923).

[6] H. Erlenmeyer, M. Simon, Helv. Chim. Acta 24, 1210 (1941).

[7] Dictionary of Organic Compounds I, 40. [Russian translation].

[8] F. Vacirca, Boll. ist. sieroterap. milanese 22, 384 (1943); Ch. A. 40, 4760 (1946).

[9] S. W. Fox, M. Winitz, Arch. Biochem. Biophys. 35, 419 (1952); Ch. A. 46, 5637 (1952).

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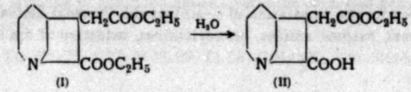
# SYNTHESIS OF 6,7-DISUBSTITUTED DERIVATIVES OF 1-AZABICYCLO-(3.2.1)-OCTANE

V. Ia. Furshtatova, E. E. Mikhlina and M. V. Rubtsov

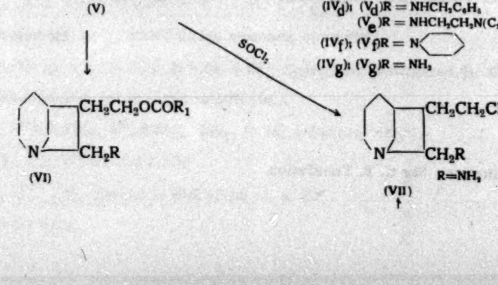
In our previous communication [1] we have described a simple method for the preparation of 6-carboxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid and of some of its derivatives.

In the course of the investigation of the chemical behavior of these compounds the properties of the ethyl ester of 6-carbethoxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid were found to be of greatest interest. Thus, it was found that this diester easily undergoes hydrolysis on standing in aqueous solution, with formation of an acid ester. As has previously been pointed out [2], this property is also exhibited by the isomeric ethyl ester of 3-carbethoxymethyl-quinuclidine-2-carboxylic acid. Under similar conditions the latter ester is transformed into 3-carbethoxymethylquinuclidine-2-carboxylic acid. A comparison of the properties of these two isomeric diesters gives reason to suppose that it is the carbethoxy group in position 7 in the ethyl ester of 6-carbethoxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid (I) which undergoes hydrolysis, and the acid ester so formed has the structure of 6-carbethoxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid (II).

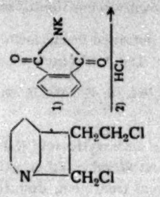

CH2COOC2H5
COOC2H5
N
(I)
H2O
CH2COOC2H5
COOH
N
(II)

Starting from the latter compound we have obtained a number of 7-alkyl-(aryl)-aminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octanes and also several esters of 7-dialkyaminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octane.

The syntheses were effected according to the following scheme:


(II)
SOCl2
CH2COOC2H5
N
COCl
HCl
(III)
CH2COOC2H5
N
COR
(IV)
LiAlH4
CH2CH2OH
N
CH2R
(V)
(IVa); (Va)R = N(C2H5)2
(IVb); (Vb)R = N(CH3)2
(IVc); (Vc)R = HN
N
(IVd); (Vd)R = NHCH2C6H5
(Ve)R = NHCH2CH2N(C2H5)2
(IVf); (Vf)R = N
(IVg); (Vg)R = NH2
SOCl2
CH2CH2OCOR1
N
CH2R
(VI)
CH2CH2Cl
N
CH2R
R=NH2
(VII)
†

(VIa) $R = N(C_2H_5)_2$, $R_1 = C_6H_5$
(VIb) $R = N(C_2H_5)_2$, $R_1 = CH_3$
(VIc) $R = N(CH_3)_2$, $R_1 = C_6H_5$
(VId) $R = N(CH_3)_2$, $R_1 = CH_3$
(VIe) $R = N(CH_3)_2$, $R_1 = CH_2CH_3$



The carboxylic acid (II) was transformed by means of thionyl chloride into the hydrochloride of the acid chloride (III) which was subsequently treated with alkyl-(aryl)-amines.

The resultant alkyl-(aryl)-amides (IV) were then reduced by means of lithium aluminum hydride to the corresponding 1-azabicyclo-(3.2.1)-octane derivatives (V). On treating the latter with certain acyl chlorides there were obtained the corresponding esters (VI). On interacting derivative ($V_g$) with thionyl chloride there was obtained the 7-aminomethyl-6-(β-chloroethyl) derivative (VII).

It must be pointed out that compound (VII) is also formed during the condensation of 7-chloromethyl-6-(β-chloroethyl)-1-azabicyclo-(3.2.1)-octane, prepared earlier [1], with potassium phthalimide and the subsequent hydrolysis of the phthalimide derivative with hydrochloric acid, which indicates a restricted lability of the chlorine atom in the 6-β-chloroethyl group.

## EXPERIMENTAL

Diethylamide of the carboxylic acid (II) (Compound IVa). 3 g of the ethyl ester of the carboxylic acid (II) was dissolved in 60 ml of water and the solution was allowed to stand at room temperature for 7 days. The water was then removed in vacuo and the residue dried by triple steam distillation with benzene. The acid ester obtained was washed several times with ether in order to remove any unhydrolyzed diester and was then dissolved in 50 ml of chloroform; the chloroform solution was filtered from the 6-carboxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid. After removing the chloroform in vacuo there remained 2.4 g (89%) of the carboxylic acid (II) in the form of a viscous oil. The acid ester obtained was heated, without further purification, with 30 ml of thionyl chloride for 4 hours at 60-75°. Excess thionyl chloride was removed in vacuo and the last traces were removed by triple distillation with benzene.

The foam-like mass representing the hydrochloride of 6-carbethoxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid chloride, was suspended in 25 ml of anhydrous ether and treated with a solution of 7 g of diethylamine in 30 ml of benzene, with cooling. The reaction mixture was allowed to stand for 1 hour after which 50% potassium hydroxide solution was added and the oil which separated extracted with benzene. The benzene extract was dried over potassium hydroxide. After removing the solvent in vacuo the residue was distilled. B. p. 151-154° at 0.3 mm. In this way there was obtained 2.2 g (75%) of the diethylamide of the carboxylic acid (II) in the form of a mobile liquid which is soluble in water and organic solvents.

Found %: C 64.61, 64.83; H 9.50, 9.35; N 9.53, 9.03. $C_{16}H_{28}O_3N_2$. Calculated %: C 64.86; H 9.46; N 9.46.

Dimethylamide of the carboxylic acid (II) (Compound IVb). By interacting the carboxylic acid (II), obtained from 2.1 g of its ethyl ester by the method described in the foregoing experiment, with thionyl chloride there was obtained the acid chloride of (II). On treating the latter with 30 ml of a 15% solution of dimethylamine in ether there was obtained 1.4 g (75.5%) of dimethylamide of the carboxylic acid (II) (Compound IVb). Brown viscous liquid, b. p. 134-141°/0.2 mm, soluble in water and organic solvents.

Found %: C 62.48, 62.04; H 8.51, 8.98. $C_{14}H_{24}O_3N_2$. Calculated %: C 62.68; H 8.95.

The methiodide was obtained as white crystals soluble in water and alcohol and insoluble in ether, m. p. 178-180°.

Found %: I 30.87, 30.42; N 6.67, 6.50. $C_{15}H_{27}O_3N_2I$ Calculated %: I 30.97; N 6.83

Pyridyl-(2')-amide of the carboxylic acid (II) (Compound IVc). The hydrochloride of the carboxylic acid (II) chloride (Compound III) prepared from 2.1 g of the diester (I) by the method described above, was treated with a solution of 4.44 g of 2-aminopyridine in 25 ml of benzene; there was obtained 1.42 g (63%) of Compound (IVc) in the form of a brown viscous liquid, soluble in water and organic solvents. B. p. 185°/0.3 mm.

The dipicrate was obtained in the form of yellow crystals which are soluble in acetone and difficultly soluble in alcohol. M. p. 188-191° (from a mixture of acetone and alcohol).

Found %: C 44.76, 44.76; H 3.69, 3.74; N 16.22, 16.22. $C_{29}H_{29}O_{17}N_9$. Calculated %: C 44.90; H 3.73; N 16.25.

Benzylamide of the carboxylic acid (II) (Compound IVd). To a mixture of compound (III) obtained from 2.1 g of the diester (I), and 25 ml of ether was added, with cooling, a solution of 5 g of benzylamine in 25 ml of benzene. After the usual treatment, described in foregoing experiment, there was obtained 2 g (87%) of compound (IVd), b. p. 178°/0.3 mm. Greenish-yellow liquid, somewhat viscous, soluble in water and organic solvents.

Found %: C 69.40, 69.42; H 7.69, 7.96; N 8.67, 8.55. $C_{19}H_{26}O_3N_2$. Calculated %: C 69.10; H 7.86; N 8.50.

N-[6-Carbethoxymethyl-1-azabicyclo-(3.2.1)-octanoyl-7]-piperidine (IVf). A mixture consisting of the hydrochloride (III), obtained from 30 g of the diester (I), 300 ml of benzene and 90 ml of piperidine was refluxed for 4 hours. Excess piperidine and solvent were removed in vacuo and the residue dissolved in 50 ml of water and treated with 50% solution of potassium hydroxide. The amide formed was extracted with benzene. After drying the benzene solution over caustic potash, the solvent was removed and the substance distilled in vacuo, b. p. 180°/0.3 mm.

The amide obtained is an oily rather viscous liquid which is soluble in organic solvents. Yield, 27.9 g (81%).

Found %: N 8.82, 8.55. $C_{17}H_{28}O_3N_2$. Calculated %: N 9.09.

Amide of carboxylic acid (II) (Compound (IVg). 14.2 g of the diester (I) was transformed into the acid chloride by the method described above. The latter was suspended in 100 ml of ether; the reaction mixture was saturated with ammonia during 1 hour, with cooling. The reaction mixture was then treated with 50% caustic potash and the amide formed extracted with benzene. After drying the benzene solution over potash and removing the solvent in vacuo there was obtained the amide (IVg) in the form of colorless crystals, m. p. 118° (from ethyl acetate), yield 2.4 g (19%).

Found %: C 60.34, 59.78; H 8.42, 8.26; N 11.74, 11.45. $C_{12}H_{20}O_3N_2$. Calculated %: C 60.00; H 8.33; N 11.66.

7-Diethylaminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octane (Va). A solution of 5 g of the diethylamide of the carboxylic acid (II) (Compound IVa) in 50 ml of anhydrous benzene was added to a suspension of 2.64 g of lithium aluminum hydride in 50 ml of anhydrous ether. The reaction mixture was refluxed for 20 hours. At the end of this period 5 ml of water was added with cooling and stirring. The lithium and aluminum hydroxides formed were filtered off and were thoroughly washed with ether. The extracts were dried over potassium hydroxide. After removing the solvent the residue, representing compound (Va), was distilled in vacuo, b. p. 140-143°/0.2 mm. Yield 3.25 g (80.5%). Mobile colorless liquid soluble in water and organic solvents.

Found %: N 11.44, 11.22. $C_{14}H_{28}ON_2$. Calculated %: N 11.66.

7-Dimethylaminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3,2,1)-octane (Vb). A solution of 2.4 g of the amide (IVb) in 30 ml of benzene was added to a suspension of 1.4 g of lithium aluminum hydride in 20 ml of ether. After refluxing the mixture for 20 hours it was treated in a manner similar to that described in the foregoing experiment. There was obtained 1.43 g (76%) of the amine (Vb) as a viscous colorless oil, soluble in water and organic solvents. B. p. 130-132°/0.3 mm.

Found %: N 12.65. $C_{12}H_{24}ON_2$. Calculated %: N 13.21.

The dipicrate was obtained as yellow crystals, soluble in alcohol and acetone; insoluble in water, benzene, ether. M. p. 64-70°.

Found %: C 42.82, 43.29; H 4.85, 4.60; N 16.68. $C_{24}H_{30}O_{15}N_8$. Calculated %: C 42.98; H 4.47; N 16.71.

The dimethiodide was obtained in the form of a white amorphous powder, soluble in water and alcohol and insoluble in ether.

Found %: N 5.92, 6.12. $C_{14}H_{30}ON_2I_2$. Calculated %: N 5.64.

7-(Pyridyl-2')-aminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octane (Vc). 1.2 g of the amide (IVc) was reduced with 0.6 g of lithium aluminum hydride. There was obtained 0.7 g (70.2%) of compound (Vc) as a yellow viscous liquid, easily soluble in organic solvents and water. B. p. 188-190°/0.3 mm.

The dipicrate is in the form of yellow crystals, soluble in alcohol and acetone, and insoluble in ether and water. M. p. 178-180°.

Found %: C 44.65, 44.75; H 4.05, 4.17; N 17.50. $C_{27}H_{29}O_{15}N_9$. Calculated %: C 45.06; H 4.05; N 17.52.

7-Benzylaminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octane (Vd). A solution of 2.1 g of the amide (IVd) in 20 ml of benzene was added to a suspension of 1 g of lithium aluminum hydride in 20 ml of ether. After heating at 60° for 20 hours 20 ml of anhydrous dioxan was added to the reaction mixture and heating was continued at reflux for another 20 hours. The reaction products were treated by the method described. There was obtained 1.4 g (80%) of Compound (Vd) as a viscous yellow oil, soluble in organic solvents and water. B. p. 194-196°/0.3 mm.

Found %: C 74.21, 74.11; H 9.31, 9.50; N 9.89. $C_{17}H_{26}ON_2$. Calculated %: C 74.45; H 9.49; N 10.21.

The dipicrate was obtained as a yellow amorphous powder, soluble in alcohol and acetone; insoluble in water, ether, benzene. M. p. 86° (decomp.).

Found %: C 47.60; H 4.60; N 15.65. $C_{29}H_{32}O_{15}N_8$. Calculated %: C 47.54; H 4.37; N 15.30.

7-Diethylaminoethylaminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octane (Ve). The hydrochloride (III), prepared from 2.1 g of the diester (I), was suspended in 25 ml of ether and the suspension was added, with cooling and stirring to a solution of 5 g of diethylaminoethylamine in 25 ml of benzene. After the usual treatment (as described for Compound IVa) there was obtained 2.1 g (89%) of diethylaminoethylamide of the carboxylic acid (II) as a brown oil which decomposed on distillation. Because of the danger of decomposition the compound was reduced with lithium aluminum hydride without further purification. The crude amide was treated with 1 g of the hydride. The amine formed was extracted with chloroform. After removing the chloroform the residue was distilled in vacuo, b. p. 175°/0.15 mm. Yield, 1 g (57%) of Compound (Ve). Brown viscous oil, soluble in organic solvents and water.

Found %: N 14.92, 15.22. $C_{16}H_{33}ON_3$. Calculated %: N 14.84.

N-[7-(β-Hydroxyethyl)-1-azabicyclo-(3.2.1)-octanomethyl-6]-piperidine (Vf). A solution of 25 g of the amide (IVf) in 250 ml of benzene was added to a suspension of 12.3 g of lithium aluminum hydride in 250 ml of benzene. The reaction mixture was refluxed for 20 hours. The amino alcohol formed was extracted with benzene, yield 17 g (85%). The substance is a yellow viscous oil easily soluble in organic solvents and water. B. p. 156-157°/0.3 mm.

Found %: N 10.96, 10.68. $C_{15}H_{28}ON_2$. Calculated %: N 11.11.

7-Aminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octane (Vg). 1.5 g of the amide (IVg) was added portion-wise to a suspension of 0.49 g of lithium aluminum hydride in a mixture of 30 ml of benzene and 20 ml of ether. The reaction mixture was treated as above, yielding 0.45 g (59%) of the amino alcohol (Vg) as a viscous liquid, soluble in organic solvents and water, b. p. 140°/0.3 mm.

The dipicrate was obtained as yellow crystals, soluble in alcohol, acetone; insoluble in water and ether. M. p. 87°.

Found %: C 41.33; H 4.36. $C_{22}H_{26}O_{15}N_8$. Calculated %: C 41.10; H 4.05.

7-Diethylaminomethyl-6-(β-benzoylhydroxyethyl)-1-azabicyclo-(3.2.1)-octane (VIa). To a solution of 1.5 g of the amino alcohol (Va) in 15 ml of anhydrous benzene was added, with cooling, 1.2 ml of benzoyl chloride. The reaction mixture was refluxed for 3 hours. The dihydrochloride of (VIa) formed was extracted from its solution in benzene with 5% hydrochloric acid. The hydrochloric acid solution was made alkaline with

50% potassium hydroxide solution and the base (VIa) extracted with ether. After drying the ether extract over potassium hydroxide and removing the solvent, the substance was distilled in vacuo, b. p. 189°/0.4 mm. Yield 1.6 g (76%). Light-yellow oil, easily soluble in organic solvents $n^{18}$D 1.5285.

Found %: C 72.42, 72.52; H 9.26, 9.17; N 8.36, 7.93. $C_{21}H_{32}O_2N_2$. Calculated %: C 72.92; H 9.3; N 8.11.

7-Diethylaminomethyl-6-(β-acetoxyethyl)-1-azabicyclo-(3.2.1)-octane (VIb). A mixture consisting of 1.9 g of compound (Va), 0.7 g of acetyl chloride and 20 ml of benzene was refluxed for 3 hours. Excess acetyl chloride and solvent were removed in vacuo and the residue – the dihydrochloride of (VIb) – was dissolved in water. The solution was made alkaline with 50% potassium hydroxide and the ether which separated was extracted with benzene. The benzene extract was dried over potassium hydroxide, the benzene removed in vacuo and the residue distilled. B. p. 118-119°/0.25 mm, yield 1.11 g (50%). Yellow viscous liquid soluble in organic solvents and water, $n^{18}$D 1.4812.

Found %: C 68.12; H 10.59; N 9.91. $C_{16}H_{30}O_2N_2$. Calculated %: C 68.09; H 10.63; N 9.93.

7-Dimethylaminomethyl-6-(β-benzoyloxyethyl)-1-azabicyclo-(3.2.1)-octane (VIc). From 2 g of the amino alcohol (Vb) and 1.5 g of benzoyl chloride there was obtained, by the method described for compound (VIa), 1.8 g (60.5%) of the ether (VIc) as a colorless somewhat viscous oil, soluble in organic solvents. B. p. 181-183°/0.4 mm.

Found %: C 71.94, 72.14; H 8.57, 8.67. $C_{19}H_{28}O_2N_2$. Calculated %: C 72.12; H 8.85.

7-Dimethylaminomethyl-6-(β-acetoxyethyl)-1-azabicyclo-(3.2.1)-octane (VId). To a solution of 2.2 g of the amino alcohol (Vb) in 20 ml of benzene was added 0.9 g of acetyl chloride. The mixture was refluxed for 2½ hours and subsequently treated by the method described for compound (VIb). There was obtained 2 g (76%) of compound (VId) in the form of a mobile colorless oil, b. p. 111-115°/0.3 mm, $n^{18}$D 1.4871.

Found %: C 65.85; H 10.16; N 10.94. $C_{14}H_{26}O_2N_2$. Calculated %: C 66.14; H 10.23; N 11.02.

7-Dimethylaminomethyl-6-(β-propionyloxyethyl)-1-azabicyclo-(3.2.1)-octane (VIe). To a solution of 2.2 g of the amino alcohol (Vb) in 30 ml of benzene was added 1.5 g of propionyl chloride. After refluxing for two hours the reaction mixture was treated in the usual way and there was obtained 1.5 g (54%) of compound (VIe). B. p. 130°/0.4 mm, $n^{16}$D 1.483. Yellow mobile liquid, soluble in water and organic solvents.

The dipicrate was obtained as yellow crystals soluble in alcohol and acetone, and insoluble in ether and water.

Found %: C 44.55; H 4.68. $C_{27}H_{34}O_{16}N_8$. Calculated %: C 44.50; H 4.68.

7-Aminomethyl-6-(β-chloroethyl)-1-azabicyclo-(3.2.1)-octane (VII). Method A. To a solution of 0.25 g of the amino alcohol (Vf) in 10 ml of benzene was added, with cooling and stirring, 10 ml to thionyl chloride. The reaction mixture was heated at 70° for two hours after which it was evaporated in vacuo and treated with 50% potassium hydroxide. The amino chloride (VII) which separated was extracted with ether. The ether extract was dried over potassium hydroxide, filtered, and the filtrate treated with 6% alcoholic solution of picric acid. The dipicrate of (VII) separated as yellow crystals, soluble in acetone, difficultly soluble in alcohol, and insoluble in water and ether. M. p. 208° (from water-acetone mixture).

Found %: C 39.94; H 3.98; N 17.11; Cl 5.29. $C_{22}H_{35}O_{14}N_8Cl$. Calculated %: C 39.99; H 3.78; N 16.96; Cl 5.37.

Method B. A mixture of 2 g (0.009 mole) of 7-chloromethyl-6-(β-chloroethyl)-1-azabicyclo-(3.2.1)-octane and 3.33 (0.018 mole) of potassium phthalimide in 30 ml of absolute alcohol was refluxed for 30 hours. At the end of this period the potassium chloride which separated was filtered off and the alcoholic solution evaporated in vacuo and the residue dissolved in 20 ml of hydrochloric acid (1:1). This solution was refluxed for 16 hours and the hydrochloric acid removed in vacuo. The dihydrochloride of (VII) thus formed was treated with 40% sodium hydroxide solution and the free base which separated was extracted with ether. The ethereal solution was treated to yield the dipicrate, m. p. 208° (from water-acetone mixture). The latter does not depress the melting point in mixture with the dipicrate obtained by method A.

Found %: C 40.24; H 4.10; N 16.87, 16.99; Cl 5.68, 5.37. $C_{22}H_{35}O_{14}N_8Cl$. Calculated %: C 39.99; H 3.78; N 16.96; Cl 5.37.

## SUMMARY

Hydrolysis of the ethyl ester of6-carbethoxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid gives 6-carbethoxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid. Starting from the latter acid a number of 7-alkyl-(aryl)-aminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octanes have been synthesized.

Certain esters of 7-dialkylaminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octanes have also been prepared.

An explanation has been given for the difference in the lability of the chlorine atom in positions 6 and 7 in 7-chloromethyl-6-(β-chloroethyl)-1-azabicyclo-(3.2.1)-octane.

## LITERATURE CITED

[1] V. Ia. Furshtatova, E. E. Mikhlina and M. V. Rubtsov, J. Gen. Chem. 28, 668 (1958).*

[2] M. V. Rubtsov, E. E. Mikhlina and V. Ia. Furshtatova, Ibid. 24, 2217 (1954).*

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* Original Russian pagination. See C. B. Translation.

# SYNTHESIS OF SUBSTITUTED QUINUCLIDINE-2-CARBINOLS

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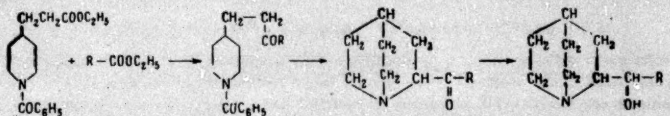
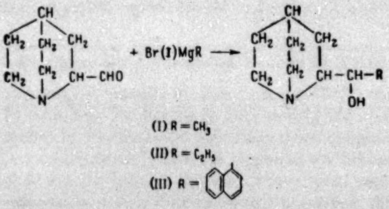
The synthesis of substituted quinuclidine-2-carbinols – compounds of the quinine alkaloid type – was first accomplished by P. Raabe in 1911 [1]. The Raabe method consists in condensing the ethyl esters of β-[N-benzoylpiperidyl-(4)]-propionic acid and of some other acid (for example, cinchoninic or quininic acids) followed by closure of the quinuclidine ring and reduction of the resultant ketone to the corresponding substituted quinuclidine-2-carbinol.



Up to the present this was the only method for the preparation of substituted quinuclidine-2-carbinols. By this method were obtained quinine [2], hydroquinone [3] as well as a number of analogs and isomers of quinine alkaloids [4-6].

The present paper describes a new method of preparation of substituted quinuclidine-2-carbinols according to the following scheme



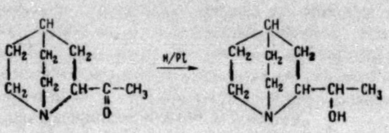
(I) R = $CH_3$

(II) R = $C_2H_5$

(III) R =

The starting material is 2-formylquinuclidine [7] which on interacting with various organomagnesium compounds gives rise to the formation of the corresponding substituted quinuclidine-2-carbinols. In this way we have prepared (quinuclidine-2)-methyl carbinol (I), (quinuclidine-2)-ethyl carbinol (II) and (quinuclidine-2)-(naphthyl-1)-carbinol (III).

(Quinuclidine-2)-methyl carbinol was also prepared by reducing 2-acetylquinuclidine [8] (IV) in the presence of platinum catalyst.



(IV) (I)

Now, reduction of compound (IV) in absolute alcohol as the solvent gives, as is also the case in the organomagnesium method, a mixture of two diastereoisomeric (quinuclidine-2)-methyl carbinols, a crystalline one and another in the form of an oil. Reduction of compound (IV) in distilled water gives only the crystalline diastereoisomer.

## EXPERIMENTAL

### (Quinuclidine-2)-Methyl Carbinol (I)

1) From 2-formylquinuclidine. To the Grignard reagent, prepared from 1.34 g of methyl iodide and 0.23 g of magnesium in anhydrous ether, was added at 0° a solution of 1.3 g of freshly prepared 2-formylquinuclidine in 10 ml of anhydrous ether. The reaction mixture was stirred at room temperature for 10 hours after which it was treated with 25 ml of 5% hydrochloric acid and extracted with ether. The hydrochloric acid solution was made alkaline with excess of 50% potassium hydroxide and the base which separated was extracted with ether. The ether extract was dried over potassium hydroxide, the ether removed and the residue distilled in vacuo. Yield 1.04 g (74.5%) of a mixture of the diastereoisomeric racemates of quinuclidine-2-methyl carbinol in the form of a colorless oil, b. p. 60° (2 mm). The substance dissolves easily in the usual organic solvents and in water; $n^{20}D$ 1.4913.

Found %: N 9.09. $C_9H_{17}ON$. Calculated %: N 9.03.

The hydrochloride was obtained as a colorless oil by treating an ethereal solution of the base with an alcoholic solution of hydrogen chloride.

The picrate forms yellow crystals melting at 173-175°.

Found %: C 46.71, 47.05; H 5.08, 5.24; N 14.71. $C_9H_{17}ON \cdot C_6H_3O_7N_3$. Calculated %: C 46.87; H 5.21; N 14.58.

In order to resolve the diastereoisomerides use was made of the difference in the solubilities of their hydrochlorides in alcohol and acetone.

0.77 g of the base (I) was mixed with 2 ml of 10% alcoholic hydrogen chloride and 10 ml of anhydrous acetone. The white crystalline precipitate which separated was filtered off and recrystallized from absolute alcohol. There was obtained 0.27 g of (quinuclidine-2)-methyl carbinol hydrochloride (racemate A). Colorless crystals, easily soluble in water, sparingly soluble in the usual organic solvents; m. p. 218-220°.

Found %: C 56.12, 55.94; H 9.41, 9.28; N 7.24, 7.03. $C_9H_{17}ON \cdot HCl$. Calculated %: C 56.39; H 9.40; N 7.31.

The free base is a colorless oil boiling at 92-95° (3 mm), $n^{20}D$ 1.5040. On standing the oil crystallizes to colorless crystals, m. p. 38°. The substance is easily soluble in water and in organic solvents.

Found %: N 8.90. $C_9H_{17}ON$. Calculated %: N 9.03.

The picrate forms yellow crystals, soluble in acetone, insoluble in alcohol and ether; m. p. 163-165°.

Found %: C 46.71, 47.05; H 5.08, 5.24; N 14.71. $C_9H_{17}ON \cdot C_6H_3O_7N_3$. Calculated %: C 46.87; H 5.21; N 14.58.

The acetone-alcoholic mother-liquor obtained after separating racemate A was evaporated in vacuo. The residue was triturated with 3 ml of anhydrous acetone. The deliquescent crystals which separated were recrystallized from absolute alcohol. After two crystallizations another 0.03 g of the hydrochloride of racemate A was obtained, m. p. 218-220°.

The acetone mother liquor was evaporated in vacuo, yielding 0.2 g of the hydrochloride of (I) (racemate B) as a colorless oil which is easily soluble in water and alcohol, difficultly soluble in acetone, and insoluble in ether.

The free base is a colorless oil easily soluble in water and organic solvents, b. p. 60° (2 mm), $n^{20}D$ 1.4871.

Found %: N 8.92. $C_9H_{17}ON$. Calculated %: N 9.03.

The picrate is formed as yellow crystals, soluble in acetone, insoluble in alcohol and ether; m. p. 183-185°.

Found %: N 14.63. $C_9H_{17}ON \cdot C_6H_3O_7N_3$. Calculated %: N 14.58.

2) From 2-acetylquinuclidine. (a) 1 g of 2-acetylquinuclidine in 20 ml of absolute alcohol was hydrogenated at 18-20° and at a pressure of 20-25 cm water gauge, in the presence of 0.1 g of platinum catalyst prepared by Adams' method. Hydrogenation was completed in three hours. The catalyst was filtered off, the filtrate evaporated and the residue distilled in vacuo. There was obtained 0.91 g (89.7%) of a mixture of the diastereoisomeric (quinuclidine-2)-methyl carbinols in the form of a colorless oil boiling at 60° (2 mm). The substance dissolves easily in organic solvents and water; $n^{20}D$ 1.4913.

The hydrochloride is formed as a colorless oil. The picrate forms yellow crystals, m. p. 173-175°.

The mixture of the diastereoisomerides was resolved into the racemates A and B by the method described above.

(b) 2.8 g of 2-acetylquinuclidine dissolved in 28 ml of distilled water was hydrogenated at a temperature of 18-20° and a pressure of 20-25 cm water gauge, in the presence of 0.3 g of platinum catalyst prepared by Adams' method. Hydrogenation was completed in three hours. The catalyst was filtered off, the filtrate evaporated in vacuo and traces of moisture removed by steam distillation with benzene. The residue was dissolved in anhydrous ether, a small amount of fluffy precipitate which formed was filtered off, the ether removed and the residue distilled in vacuo. There was obtained 2.05 g (72.5%) of racemate A of (quinuclidine-2)-methyl carbinol. Colorless oil, b. p. 92-95° (3 mm), $n^{20}D$ 1.5040. On standing the substance crystallized in the form of white crystals melting at 38°.

The hydrochloride forms colorless crystals, m. p. 218-220°. The picrate is formed as yellow crystals, m. p. 163-165°.

(Quinuclidine-2)-ethyl carbinol (II) was prepared by the method using the Grignard reagent in a manner similar to that employed in the preparation of (quinuclidine-2)-methyl carbinol. From 1.3 g of freshly prepared 2-formylquinuclidine, 1.4 g of ethyl bromide and 0.32 g of magnesium there was obtained 0.8 g (50.9%) of a mixture of the diastereoisomeric racemates of (II). Colorless oil, b. p. 100-110° (45 mm). The substance is easily soluble in water and organic solvents; $n^{20}D$ 1.4883.

Found %: N 8.14. $C_{10}H_{19}ON$. Calculated %: N 8.28.

The hydrochloride is an oil. The picrate is formed as yellow crystals melting at 149-150° from a mixture of alcohol and ether.

Found %: C 48.10; H 5.76; N 14.04, 14.18. $C_{10}H_{19}ON \cdot C_6H_3O_7N_3$. Calculated %: C 48.29; H 5.54; N 14.07.

(Quinuclidine-2)-(naphthyl-1)-carbinol (III). To 0.26 g of magnesium turnings activated by heating with a few crystals of iodine, was added a solution of 2.23 g of α-bromonaphthalene in 10 ml of anhydrous ether over a period of 45 minutes. The reaction mixture was refluxed for 4 hours. To the naphthyl magnesium bromide so obtained was added, at 0°, a solution of 1.6 g of freshly prepared 2-formylquinuclidine in 2 ml of anhydrous ether. The reaction mixture was stirred for 14 hours at room temperature, after which it was treated with 50 ml of 5% hydrochloric acid. Nonbasic constituents of the mixture were separated by extraction with ether. The hydrochloric acid solution was then made alkaline with 50% potassium hydroxide, the base which separated was extracted several times with ether and the extract, after drying over potassium hydroxide, was evaporated to a volume of 25 ml. After standing for two days there crystallized 0.1 g of a substance which was recrystallized from anhydrous acetone as colorless needles, m. p. 200-201°. The substance dissolves in alcohol and acetone, is difficultly soluble in ether and insoluble in water.

The hydrochloride forms colorless crystals melting at 203.5-205.5°. It is easily soluble in water, alcohol, chloroform and acetone, and insoluble in ether.

The base and its hydrochloride are identical, respectively, with the base and the hydrochloride of racemate A of (quinuclidine-2)-(naphthyl-1)-carbinol prepared earlier by Raabe's method from β-[N-benzoylpiperidyl-(4)]-propionic acid and α-naphthoic acid [5].

The ethereal mother liquor left after separation of racemate A was evaporated in vacuo. The residue was distilled at a pressure of 0.4 mm. Two fractions were collected: fraction 1 (0.8 g), boiling at 60-80° was identified as unreacted 2-formylquinuclidine, fraction No. 2 (0.45 g) boiling at 192-195°, constituted a mixture of the diastereoisomers of (III) in the form of a viscous oil. In order to resolve the diastereoisomerides the oil was triturated with anhydrous ether. The crystalline product which separated (0.18 g) melted at 200-201° after recrystallization from anhydrous acetone and did not give melting point depression in mixture with racemate A of (III).

The ethereal solution obtained after separating racemate A was evaporated in vacuo. The residue (0.23 g) crystallized on standing in the dessicator over caustic potash. For the purpose of further purification the compound was transformed into its hydrochloride. This was triturated with anhydrous acetone. There were obtained colorless crystals melting at 275° (decomp.). The free base liberated from the hydrochloride was in the form of an oil which crystallized on standing in a vacuum-dessicator over potassium hydroxide. The crystals melt at 64-67°*. The substance dissolves easily in alcohol, acetone, chloroform and ether.

The hydrochloride forms colorless crystals melting at 289-290°* (after two recrystallizations from alcohol). It is soluble in water, alcohol, chloroform; insoluble in acetone and ether.

Found %: C 70.72; H 7.40. $C_{18}H_{21}ON \cdot HCl$. Calculated %: C 71.14; H 7.30.

The compounds thus synthesized are, respectively, the free base, (quinuclidine-2)-(naphthyl-1)-carbinol (racemate B), and its hydrochloride, both of which have been prepared earlier [5] by Raabe's method from the ethyl esters of β-[N-benzoylpiperidyl-(4)]-propionic and α-naphthoic acids.

The combined yield of racemates A and B of (III) was 35.3% (based on the 2-formylquinuclidine).

## SUMMARY

1. A new method for the synthesis of substituted quinuclidine-2-carbinols from 2-formylquinuclidine and organomagnesium compounds has been described.

2. (Quinuclidine-2)-methyl carbinol, (quinuclidine-2)-ethyl carbinol and (quinuclidine-2) (naphthyl-1)-carbinol have been synthesized by the method outlined.

3. (Quinuclidine-2)-methyl carbinol has also been prepared by reduction of 2-acetylquinuclidine in the presence of a platinum catalyst. In this case a mixture of the two diastereoisomerides has been obtained when reduction was effected in absolute alcohol, just as is the case in the synthesis using the Grignard reagents; reduction in water, however, gave rise to the formation of only one of the two diastereoisomerides.

## LITERATURE CITED

[1] P. Raabe, Ber. 44, 2088 (1911); P. Raabe, K. Kindler, Ber. 51, 1360 (1918).

[2] R. B. Woodward, W. E. Doering, J. Am. Chem. Soc. 66, 849 (1944); 67, 860 (1945).

[3] P. Raabe, et al., Ber. 64, 2487 (1931).

[4] M. V. Rubtsov, J. Gen. Chem. 9, 1493 (1939); 13, 593, 702 (1943); 16, 461 (1946); G. R. Clemo, S. P. Popli, J. Chem. Soc. 1951, 1406.

[5] M. V. Rubtsov and V. A. Volskova, J. Gen. Chem. 23, 1893 (1953).**

[6] M. V. Rubtsov and V. A. Volskova, Ibid. 23, 1685 (1953).**

[7] M. V. Rubtsov and L. N. Iakhontov, Ibid. 25, 2143, (1955).**

[8] M. V. Rubtsov and L. N. Iakhontov, Ibid. 27, 72 (1957).**

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* In the paper [5] it was indicated that racemate B of (quinuclidine-2)-(naphthyl-1)-carbinol melts at 63-65° and its hydrochloride at 267.5-269°.

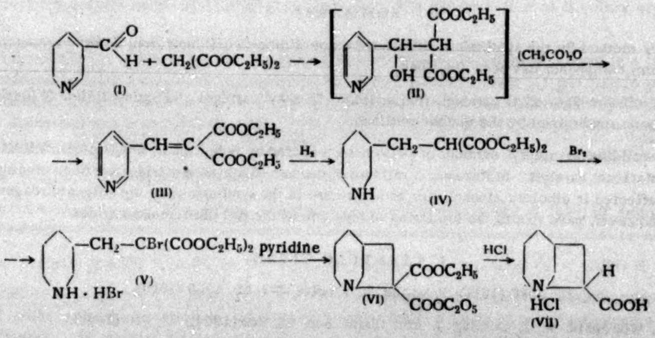
** Original Russian pagination. See C. B. Translation.

# THE SYNTHESIS OF 1-AZABICYCLO-[3.2.1]-OCTANE-7-CARBOXYLIC ACID

A. K. Chizhov and M. V. Rubtsov

The information in the literature on 1-azabicyclo-[3.2.1]-octanes is limited to the description of the synthesis of the unsubstituted bicyclic compound [1] and some of its 6-substituted derivatives [2,3]. Definite interest is offered by the synthesis of the unknown 1-azabicyclo-[3.2.1]-octanes with substituents in the 7 position, inasmuch as the latter are isomeric with the 2-substituted derivatives of quinuclidine (1-azabicyclo-[2.2.2]-octane), to which the quinine alkaloids and a number of other compounds obtained in recent years are related. Among these compounds are found substances with valuable biological properties.

The present work is devoted to the synthesis of 1-azabicyclo-[3.2.1]-octane-7-carboxylic acid, which in turn can serve as the starting material for the preparation of 7-substituted derivatives of 1-azabicyclo-[3.2.1]-octane. The synthesis of the acid was accomplished by the following scheme



Nicotinic aldehyde (I) was condensed with malonic ester in the presence of piperidine at room temperature; in this way the diethyl ester of 2-(pyridyl-3')-2-hydroxyethane-1,1-dicarboxylic acid (II) was produced. Heating of the diester (II) with acetic anhydride resulted in the splitting out of a molecule of water and the formation of the diethyl ester of 2-(pyridyl-3')-vinyl-1,1-dicarboxylic acid (III). The hydrochloride of the diester (III) was further subjected to reduction in alcohol solution in the presence of platinic oxide (according to Adams' method), whereupon the hydrochloride of the diethyl ester of 2-(piperidyl-3')-ethane-1,1-dicarboxylic acid (IV) was obtained. For the subsequent transition from the 3-substituted piperidine to the azabicyclic system, compound (IV) was treated with bromine in chloroform solution. The diethyl ester of 2-(piperidyl-3')-1-bromoethane-1,1-dicarboxylic acid (V) which was formed was converted by heating with pyridine to 7,7-dicarboethoxy-1-azabicyclo-[3.2.1]-octane (VI). Boiling the diester (VI) with concentrated hydrochloric acid led to the formation of the hydrochloride of 1-azabicyclo-[3.2.1]-octane-7-carboxylic acid (VII).

## EXPERIMENTAL

Diethyl ester of 2-(pyridyl-3')-vinyl-1,1-dicarboxylic acid (III). 17.0 g. of nicotinic aldehyde, 181.3 g of malonic ester, and 1.5 g of piperidine were allowed to stand at 20° for 7 days. The unreacted malonic ester and piperidine were distilled off in vacuo. To the residue, which consisted of the diethyl ester of 2-(pyridyl-3')-2-hydroxyethane-1,1-dicarboxylic acid was added 94.2 g of acetic anhydride and the mixture was heated for 2 hours at 115-117°. Then the acetic anhydride and acetic acid were distilled off in vacuo, and the remaining material was distilled at 0.25 mm and the fraction was collected that boiled within the limits 130-136°. Yield of diethyl ester (III) 30.6 g (77.5%), $n^{20}D$ 1.5275. Colorless liquid, soluble in ether, insoluble in water.

Found %: C 62.01; H 6.28. $C_{13}H_{15}O_4N$. Calculated %: C 62.63; H 6.06.

**Hydrochloride** – white, crystalline powder with m. p. 152-153°. Readily soluble in water and alcohol.

**Diethyl ester of 2-(piperidyl-3')-ethane-1,1-dicarboxylic acid (IV).** To a solution of 11.58 g of the hydrochloride of the diethyl ester of 2-(pyridyl-3')-vinyl-1,1-dicarboxylic acid in 130 ml of anhydrous alcohol was added 0.51 g of platinic oxide prepared according to the method of Adams. The reaction mixture was shaken with hydrogen at room temperature. The hydrogenation was completed in 10 hours. The platinum black was filtered off and the alcoholic solution was evaporated in vacuo at 40°. The hydrochloride of the diethyl ester of 2-(piperidyl-3')-ethane-1,1-dicarboxylic acid was obtained as an extremely hygroscopic, viscous, caramel-like mass, readily soluble in chloroform. Quantitative yield.

To isolate the base, 8.18 g of the hydrochloride of the diethyl ester of 2-(piperidyl-3')-ethane-1,1-dicarboxylic acid was treated with 20 ml of 50% aqueous potassium carbonate solution. The oil that separated was extracted with ether, the extract was dried with potassium carbonate, the ether was distilled off in vacuo, and the residue was subjected to vacuum distillation. Yield of diethyl ester (IV) 4.54 g (63.5%).

B. p. 125-126° (0.3 mm), $n^{20}D$ 1.4638, $d^{20}_4$ 1.0599, $MR_D$ 66.41; calculated 66.94.

Found %: N 5.38, 5.56. $C_{13}H_{23}O_4N$. Calculated %: N 5.46.

**7,7-Dicarboethoxy-1-azabicyclo-[3.2.1]-octane (VI).** To a solution of 12.13 g of the hydrochloride of the diethyl ester of 2-(piperidyl-3')-ethane-1,1-dicarboxylic acid in 36 ml of dry chloroform was added over a period of 12 hours a solution of 8.8 g of bromine in 101 ml of dry chloroform at room temperature. The mixture was stirred for 2 hours longer, after which the chloroform was distilled off in vacuo at 35-40°. To the oily residue was added 5 times its volume of absolute ether. After trituration and 4 hours' standing at room temperature the oil crystallized. The crystals were filtered off, washed with ether, and dried in the air. Yield of hydrobromide of the diethyl ester of 2-(piperidyl-3')-1-bromoethane-1,1-dicarboxylic acid 17.8 g. The compound formed yellowish crystals, readily soluble in water, difficultly soluble in ether. M. p. 90-92°.

12.53 g of the hydrobromide of the diethyl ester of 2-(piperidyl-3')-1-bromoethane-1,1-dicarboxylic acid was suspended in 12 ml of water and 12 ml of 50% aqueous potassium carbonate solution was added. The base that separated was extracted with ether, the ethereal extract was evaporated in vacuo, and the residue was dissolved in 51 ml of dry pyridine. The pyridine solution was heated to boiling for 2 hours. Then the pyridine was evaporated in vacuo. To the residue was added 8.3 ml of 50% aqueous potassium carbonate solution and the resulting mixture was extracted with ether. The ethereal extract was dried with potassium carbonate, the ether was distilled off, and the remaining material was distilled in vacuo. A fraction was collected that boiled at 152-154° (5 mm). Yield 4.44 g (57.8%). It should be noted that the fraction that distilled below 152° had the same refractive index and upon hydrolysis with hydrochloric acid yielded the hydrochloride of 1-azabicyclo-[3.2.1]-octane-7-carboxylic acid.

$n^{20}D$ 1.4770, $d^{20}_4$ 1.1104, $MR_D$ 64.97; calculated 65.08.

Found %: C 61.28; H 8.12. $C_{13}H_{21}O_4N$. Calculated %: C 61.15; H 8.28

**Hydrochloride of 1-azabicyclo-[3.2.1]-octane-7-carboxylic acid (VII).** 3.4 g of 7,7-dicarboethoxy-1-azabicyclo-[3.2.1]-octane and 35 ml of concentrated hydrochloric acid were refluxed for 8 hours. The hydrochloric acid solution was evaporated on a steam bath until crystallization began. The residue was cooled to room temperature and after standing for an hour and a half the crystals that were obtained were diluted with acetone and filtered. 2.41 g (94.5%) of the hydrochloride of 1-azabicyclo-[3.2.1]-octane-7-carboxylic acid was obtained. M. p. 273-274°. After recrystallization from a mixture of alcohol and ether, m. p. 290-293°.

Found %: C 50.40; H 7.41; N 7.38, 7.26; Cl 18.63. $C_8H_{13}O_2N \cdot HCl$. Calculated %: C 50.15; H 7.37; N 7.31; Cl 18.51.

## SUMMARY

The synthesis of the hydrochloride of 1-azabicyclo-[3.2.1]-octane-7-carboxylic acid has been carried out, starting from nicotinic aldehyde through the diethyl ester of 2-(pyridyl-3')-vinyl-1,1-dicarboxylic acid, the diethyl ester of 2-(piperidyl-3') ethane-1,1-dicarboxylic acid, and 7,7-dicarboethoxy-1-azabicyclo-[3.2.1]-octane.

## LITERATURE CITED

[1] V. Prelog, S. Heimbach, E. Cerkovnikov, J. Chem. Soc. 1939, 677; V. Prelog, K. Balenovic, Ber. 74, 1510 (1941).

[2] L. Sternbach, S. Kaiser, J. Am. Chem. Soc. 74, 2215 (1952); L. Sternbach, S. Kaiser, J. Am. Chem. Soc. 74, 2219 (1952); L. Sternbach, S. Kaiser, J. Am. Chem. Soc. 75, 6068 (1953).

[3] English patent 694067 (1953); L. Sternbach, Ch. A. 48, 114981 (1954).

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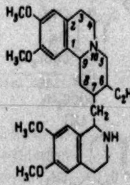
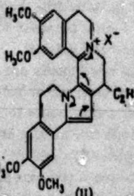
# INVESTIGATIONS IN THE ISOQUINOLINE SERIES

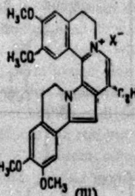
## XII. SYNTHESIS OF 4',5'-DIMETHOXY-5,6-DIMETHYL-7-(1''-METHYL-6'',7''-DIMETHOXY-1'',2'',3'',4''-TETRAHYDROISOQUINOLYL)-3,4,5,6,7,8-HEXAHYDROBENZO[1',2':1,2]QUINOLIZINE

R. P. Evstigneeva, N. M. Kashnikova, M. S. Bainova and N. A. Preobrazhenskii

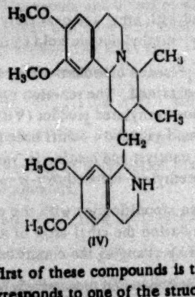
One of the interesting properties of the alkaloid emetine (I) is its ability to be converted by the action of mild oxidizing agents to a red compound, so-called rubremetine [1-3]. The structure of the latter has not been established up to the present time, although several ideas have been expressed concerning this problem [4-8].

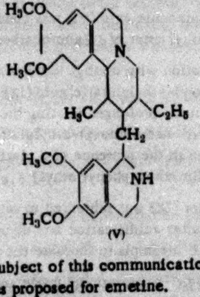

(I)


(II)


(III)

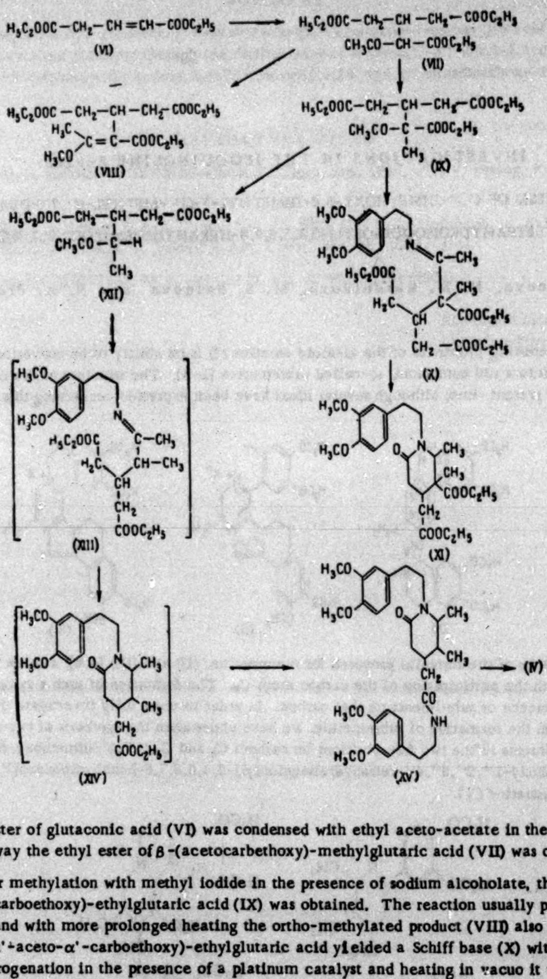
The most probable of the formulas proposed for rubremetine, (II) and (III) [6,8], assume the formation of a new ring system with the participation of the carbon atom $C_8$. The formation of such a system obviously would be difficult in the presence of substituents on that carbon. In order to more fully investigate the effect of substituents in the ring on the formation of rubremetine, we have undertaken the synthesis of two analogs of emetine that have alkyl substituents in the two free positions on carbons $C_8$ and $C_9$:1)4',5'-dimethoxy-5,6-dimethyl-7-(1''-methyl-6'',7''-dimethoxy-1'',2'',3'',4''-tetrahydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenzo[1',2':1,2]quinolizine (IV) and 2) 8-methylemetine (V).


(IV)


(V)

The synthesis of the first of these compounds is the subject of this communication. Compound (IV) is interesting also because it corresponds to one of the structures proposed for emetine.

The synthesis was based on a scheme developed for emetine [9].



The ethyl ester of glutaconic acid (VI) was condensed with ethyl aceto-acetate in the presence of sodium ethylate. In this way the ethyl ester of β-(acetocarbethoxy)-methylglutaric acid (VII) was obtained.

By its further methylation with methyl iodide in the presence of sodium alcoholate, the ethyl ester of β-(α'-aceto-α'-carboethoxy)-ethylglutaric acid (IX) was obtained. The reaction usually proceeded over a period of 1 hour, and with more prolonged heating the ortho-methylated product (VIII) also was obtained. The ethyl ester of β-(α'-aceto-α'-carboethoxy)-ethylglutaric acid yielded a Schiff base (X) with homoveratrylamine. After hydrogenation in the presence of a platinum catalyst and heating in vacuo it was converted to the ethyl ester of N-[β'-(3,4-dimethoxyphenyl)ethyl]-δ,ε-dimethyl-α-carboethoxy-α-piperidone-γ-acetic acid (XI).

The tricarboxylic ester (IX) was subjected to selective saponification with the calculated amount of sodium alcoholate and water, and after acidification and decarboxylation the ethyl ester of β-(α'-aceto)ethylglutaric acid (XII) was obtained. All attempts to increase the yield by changing the conditions were futile.

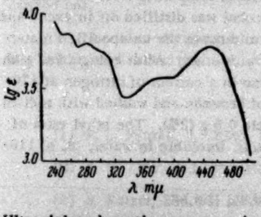
The ethyl ester of β-(α'-aceto)ethylglutaric acid was condensed successively with two molecules of homoveratrylamine without separating the intermediate products. The first molecule of homoveratrylamine reacted under the usual conditions when the reagents were mixed. The Schiff base (XIII) that was produced was hydrogenated in the presence of platinum catalyst, and the reduction product was cyclicized to the corresponding piperidone (XIV) by heating on a boiling water bath in vacuo. The latter compound was condensed with the second molecule of homoveratrylamine by heating to 180° for 1 hour. The diamide (XV) was isolated as a thick yellow oil.

After cyclization with phosphorus oxychloride and reduction of the chloride, 4',5'-dimethoxy-5,6-dimethyl-7-(1''-methyl-6'',7''-dimethoxy-1'',2'',3'',4''-tetrahydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenzo[1',2':1,2] quinolizine (IV) was obtained as a thick, light yellow oil. The hydrochloride of compound (IV) was isolated in an amorphous condition. The base 4',5'-dimethoxy-5,6-dimethyl-7-(1''-methyl-6'',7''-dimethoxy-1'',2'',3'',4''-tetrahydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenzo[1',2':1,2]quinolizine was oxidized with bromine. An orange-red substance separated, which was similar to rubremetine in physicochemical properties and absorption spectrum (Fig. 1).

Thus, the presence of an alkyl substituent on carbon atom $C_5$ did not prevent the formation of a rubro-compound.

## EXPERIMENTAL

Ethyl ester of β-(acetocarboethoxy)methylglutaric acid (VII). To a mixture consisting of 21 g of ethyl glutaconate, 29.6 g of freshly distilled acetoacetic ester, and 20 ml of anhydrous ethyl alcohol there was added, with heating, 1/6 part every 2 hours of a solution of sodium ethylate prepared from 1.5 g of sodium and 20 ml of anhydrous ethyl alcohol. Heating was continued for 12 hours. When the reaction was ended, the alcohol was distilled off in vacuo, and 30 ml of ice water was added to the residue. The oil that separated was extracted with 100 ml of ether. After the extract had been dried with sodium sulfate, the solvent was distilled off and the residue was distilled. Yield 22.6 g (63.3%). The ethyl ester of β-(acetocarboethoxy) methylglutaric acid was a colorless liquid, soluble in alcohol, ether, and benzene, insoluble in water.



Ultraviolet absorption spectrum in alcohol of the product of oxidation of compound (IV) with bromine.

B. p. 167-169° (2.5-3 mm), $d^{20}_4$ 1.1007, $n^{20}D$ 1.4500, $MR_D$ 77.27; calculated 76.44 (for the keto form), 77.49 (for the enol form).

Found %: C 56.89, 57.12; H 7.33, 7.58; $C_{15}H_{24}O_7$. Calculated %: C 56.93; H 7.65.

Ethyl ester of β-(α'-aceto-α'-carboethoxy)ethylglutaric acid (IX). To a solution of sodium ethylate prepared from 1.43 g of sodium and 29 ml of anhydrous ethyl alcohol were added 16 g of the ethyl ester of β-(acetocarboethoxy)methylglutaric acid and 21.3 g of methyl iodide. The reaction mass was heated to boiling for 1 hour. The alcohol was distilled off in vacuo, and 30 ml of water was added to the residue. The oil that separated was extracted with ether. The extract was dried with sodium sulfate. After the solvent was distilled off, the residue was distilled. Yield 11.6 g (69.4%). The ethyl ester of β-(α'-aceto-α'-carboethoxy)ethylglutaric acid was a colorless liquid, soluble in organic solvents, insoluble in water.

B. p. 149-151° (1.4 mm), $d^{20}_4$ 1.1108, $n^{20}D$ 1.4591, $MR_D$ 81.13; calculated 81.06.

Found %: C 58.29, 57.92; H 7.66, 7.95. $C_{16}H_{26}O_7$. Calculated %: C 58.14; H 7.94.

Upon more prolonged heating of the reaction mass (2.5-3 hours) the ortho-methylated product (VIII) also was obtained in considerable amounts.

B. p. 159-160° (1.5 mm), $d^{20}_4$ 1.1084, $n^{20}D$ 1.4638, $MR_D$ 82.22; calculated 82.22.

Found %: C 58.41, 58.15; H 7.98, 7.69. $C_{16}H_{26}O_7$. Calculated %: C 58.14; H 7.94.

Ethyl ester of N-[β'-(3,4-dimethoxyphenyl)ethyl]-δ,ε-dimethyl-δ-carboethoxy-α-piperidone-γ-acetic acid (XI). 5 g of the ethyl ester of β-(α'-aceto-α'-carboethoxy)ethylglutaric acid was mixed with 8.25 g of β-(3,4-dimethoxyphenyl)ethylamine. The next day the reaction mass was heated to 70° for 30 minutes. Upon cooling, it was dissolved in 25 ml of anhydrous ethyl alcohol, glacial acetic acid was added until there was a neutral reaction, and the mixture was hydrogenated in the presence of 0.3 g of platinic oxide at 30 atm for 4 hours. The catalyst was filtered off, the alcohol was distilled off, and the residue was heated in vacuo on a boiling water bath for 1 hour. Upon cooling, the reaction mass was dissolved in ether and washed with 5% hydrochloric acid solution, then with sodium bicarbonate solution. The extract was dried with sodium sulfate. The solvent was distilled off and the residue was distilled. Yield 24 g (35.4%). The ethyl ester of N-[β'-(3,4-dimethoxyphenyl)ethyl]-δ,ε-dimethyl-δ-carboethoxy-α-piperidone-γ-acetic acid was a thick, oily liquid with a yellow color, readily soluble in organic solvents. B. p. 208-210° (0.3 mm).

Found %: C 64.36, 64.29; H 7.86, 8.07; N 3.33, 3.30. $C_{24}H_{35}O_7N$. Calculated %: C 64.12; H 7.85; N 3.11.

The Schiff base (X) separated in the crystalline condition on prolonged standing. After recrystallization from anhydrous ethyl alcohol it melted at 88-89°.

Found %: C 63.49; H 7.72; N 3.01. $C_{26}H_{39}O_8N$. Calculated %: C 63.25; H 7.97; N 2.84.

Ethyl ester of β-(α'-aceto)ethylglutaric acid (XII). To a solution of sodium alcoholate prepared from 1.9 g of sodium and 36.5 ml of anhydrous ethyl alcohol were added 25.2 g of the ethyl ester of β-(α'-aceto-α'-carboethoxy)ethylglutaric acid and 1.41 g of water. The mixture was kept at room temperature for 12 hours and then heated to boiling for 1 hour. Upon cooling of the mixture, the excess alcohol was distilled off in vacuo and 18 ml of water was added to the residue. The solution was shaken with ether to remove the unsaponified material, and the aqueous layer was acidified with hydrochloric acid and extracted with ether. After being dried with sodium sulfate, the solvent was distilled off and the residue was heated in vacuo in a current of nitrogen at 170-180° for 40 minutes. Upon cooling, the reaction mass was dissolved in 40 ml of benzene and washed with sodium bicarbonate. The benzene was distilled off and the residue was distilled. Yield 0.6 g (3%). The ethyl ester of β-(α'-aceto)ethylglutaric acid was a colorless liquid, soluble in organic solvents, insoluble in water. B. p. 110-112° (1.1 mm).

Found %: C 60.80, 60.33; H 8.25, 8.37. $C_{13}H_{22}O_5$. Calculated %: C 60.42; H 8.58.

β''-(3'',4''-Dimethoxyphenyl)ethylamide-N-[β-(3',4'-dimethoxyphenyl)-ethyl]-δ,ε-dimethyl-α-piperidone-γ-acetic acid (XV). 0.55 g of the ethyl ester of β-(α'-aceto)ethylglutaric acid was mixed with 0.38 g of β-(3,4-dimethoxyphenyl)ethylamine; thereupon evolution of heat was observed. The mixture was left at room temperature overnight. Then 10 ml of anhydrous ethyl alcohol was added to the reaction mass and it was hydrogenated in the presence of 0.2 g of platinic oxide at a hydrogen pressure of 0.5 atm. The excess alcohol was distilled off and the residue was heated on a boiling water bath in vacuo for 1 hour. The piperidone derivative formed was not isolated but was heated with 0.43 g of β-(3,4-dimethoxyphenyl)ethylamine at 180° for 1 hour. Upon cooling, the reaction mass was carefully washed with dry ether and dried in a dessicator. Yield 0.9 g (82%). The diamide (XV) was a thick yellow oil, readily soluble in alcohol, difficultly soluble in toluene, insoluble in ether and water.

Found %: N 5.81, 5.51. $C_{29}H_{40}O_6N_2$. Calculated %: N 5.46.

Hydrochloride of 4',5'-dimethoxy-5,6-dimethyl-7-(1''-methyl-6'',7''-dimethoxy-1'',2'',3'',4''-tetrahydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenzo-[1',2':1,2]quinolizine (IV). A solution of 0.9 g of β''-(3'',4''-dimethoxyphenyl)ethylamido-N-[β-(3',4'-dimethoxyphenyl)ethyl]-δ,ε-dimethyl-α-piperidone-γ-acetic acid in 5 ml of toluene and 7 ml of phosphorus oxychloride was heated to gentle boiling for 1 hour. Upon cooling, the excess oxychloride and toluene was distilled off in vacuo. The residue was dissolved in 13 ml of 6% hydrochloric acid. The solution was evaporated to dryness in vacuo. The remaining thick, dark yellow oil was dissolved in anhydrous ethyl alcohol and treated with an alcoholic solution of ammonia. A precipitate of inorganic salts was filtered off. The alcoholic solution was placed in an autoclave and hydrogenated in the presence of 2 g of Raney nickel catalyst at 110 atm and 75-80° for 1.5 hours. The catalyst was filtered off and the alcohol was distilled off in vacuo. The residue was dissolved in 8 ml of water and treated, while cooling, with 5% sodium hydroxide solution. The oil that separated was extracted with ether. After being dried with potassium carbonate, the ether was distilled off. The residue was a light yellow oil (0.5 g). The hydrochloride was obtained from the ether solution of the base by treating it with ether saturated with dry hydrogen chloride. It was a colorless, amorphous substance, readily soluble in alcohol and water, insoluble in ether. M. p. 134-135° (it deformed at 112-116°).

Found %: N 4.72, 4.74. $C_{29}H_{40}O_4N_2 \cdot 2HCl$. Calculated %: N 4.79.

Oxidation of compound (IV) with bromine. To a solution of 0.1 g of the base 4',5'-dimethoxy-5,6-dimethyl-7-(1''-methyl-6'',7''-dimethoxy-1'',2'',3'',4''-tetrahydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenzo[1',2':1,2]-quinolizine in 0.3 ml of chloroform was gradually added a solution of 0.04 ml of bromine in 1.5 ml of chloroform. In 10 minutes, the mixture was treated with ammonia solution until a turbidity appeared. The chloroform solution was dried with potassium carbonate. After the solvent was distilled off, the compound was extracted with hot water. The extract was evaporated to dryness. The residue was dissolved in anhydrous alcohol. When absolute ether was added, an orange-red precipitate separated out. After repeated reprecipitation of the material from alcohol the m. p. was 164-180° (it deformed at 160°).

$\lambda_{max}$ 286 mμ, lg ε (3.80); 445-455 mμ, lg ε (3.78); $\lambda_{min}$ 270 mμ, lg ε (3.78); 340 mμ, lg ε (3.44).

Found %: N 5.09, 4.61. $C_{29}H_{33}O_4N_2Br$. Calculated %: N 5.06.

## SUMMARY

1. The synthesis of 4',5'-dimethoxy-5,6-dimethyl-7-(1''-methyl-6'',7''-dimethoxy-1'',2'',3'',4''-tetrahydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenzo-[1',2':1,2]quinolizine, an analog of emetine, has been carried out.

2. The rubro-compound has been obtained by oxidation of the emetine analog with bromine, and in this way it has been shown that a substituent on carbon atom $C_5$ does not prevent formation of the rubremetine analog.

## LITERATURE CITED

[1] F. L. Pyman, J. Chem. Soc. 1917, 419.

[2] F. H. Carr, F. L. Pyman, J. Chem. Soc. 1914, 1591.

[3] P. Karrer, Ber. 49, 2057 (1916).

[4] P. Karrer, C. H. Eugster, O. Rüttner, Helv. Chim. Acta 31, 1219 (1948).

[5] P. Karrer, O. Rüttner, Helv. Chim. Acta 33, 291 (1950).

[6] A. R. Battersby, H. T. Openshaw, H. C. S. Wood, J. Chem. Soc. 1952, 391.

[8] R. E. Tietz, W. E. McEven, J. Am. Chem. Soc. 75, 4945 (1953).

[9] R. P. Evstigneeva, R. S. Livshits, L. I. Zakharkii, M. S. Bainova, and N. A. Preobrazhenskii, Proc. Acad. Sci. USSR 75, 539 (1950); J. Gen. Chem. 22, 1467 (1952).*

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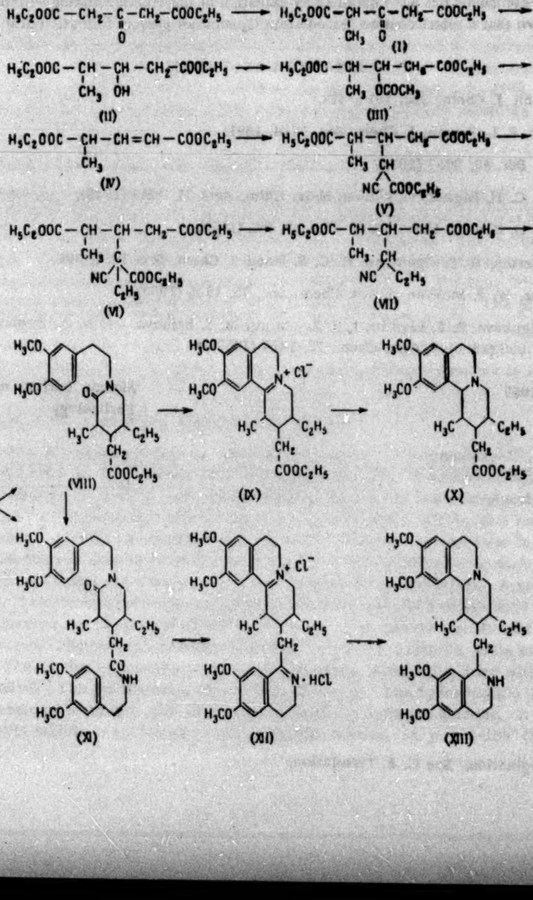
# INVESTIGATIONS IN THE ISOQUINOLINE SERIES

## XIII. SYNTHESIS OF 8-METHYLEMETINE

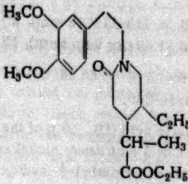
R. P. Evstigneeva, L. V. Lavrova, Ts. D. Zarankina and N. A. Preobrazhenskii

**The synthesis of 8-methylemetine was undertaken for the purpose of clarifying the effect of an alkyl substituent on carbon atom $C_8$ in the emetine molecule on the formation of the rubro-compound. For the preparation of 8-methylemetine a scheme was used that had been developed for emetine [1].**



The ethyl ester of acetonedicarboxylic acid was converted by treatment with methyl iodide in the presence of sodium alcoholate to the ethyl ester of α-methylacetonedicarboxylic acid (I). By reduction of the latter in the presence of Raney nickel catalyst the ethyl ester of α-methyl-β-hydroxyglutaric acid (II) was obtained.

The latter upon acetylation with acetic anhydride formed the ethyl ester of α-methyl-β-acetoxyglutaric acid (III). When the acetoxy derivative was heated with potassium acetate the ethyl ester of α-methylglutaric acid (IV) was produced. Further condensation with cyanoacetic ester in the presence of sodium alcoholate led to the ethyl ester of α-methyl-β-(cyano-carboethoxy) methylglutaric acid (V). By treatment with ethyl iodide and sodium alcoholate the latter was converted to the ethyl ester of α-methyl-β-(α'-cyano-α'-carboethoxy) propylglutaric acid (VI). After selective saponification with the calculated amount of sodium alcoholate and water, the ethyl ester of α-methyl-β-(α'-cyano)propylglutaric acid (VII) was obtained. Further reductive condensation of this compound with homoveratrylamine led to the piperidone derivative, which might have the structure (VIII) or (XIV).



(XIV)

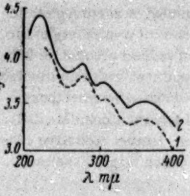
Usually reactions of such a type proceed in the direction of the compounds containing the greatest number of substituents in the ring [2,3], i.e., in the case under consideration we should obtain the piperidone (VIII). Its b. p. 198-199° (0.1 mm) indicated the formation of an individual compound, and not a mixture. The piperidone was converted to the quinolizine derivative (X) by cyclization with phosphorus oxychloride and reduction of the quaternary chloride (IX) obtained in the presence of Raney nickel catalyst. The quinolizine base was isolated as an oil. The anhydrous hydrochloride was an amorphous material; the crystal hydrate was a crystalline substance.

We attempted to demonstrate the position of the methyl group by carrying out an ester condensation of the piperidone (VIII) or the quinolizine derivative (X) with ethyl formate. The reaction did not take place in either case. The negative result could be explained either by the presence of the methyl group not in the ring, but on the side chain, or by steric hindrances occasioned by the presence of a substituent in the ortho position. Ester condensation with the formate also did not occur in the case of the ethyl ester of 4',5'-dimethoxy-6-ethyl-3,4,5,6,7,8-hexahydrobenzo-(1',2':1,2)-quinolizyl-7-acetic acid, in which the methyl group is absent. The negative result in this case is dependent, apparently, on steric hindrances. Accordingly, the reaction in the first instance, most probably, also does not occur because of steric hindrances and consequently structure (VIII) should be accepted for the piperidone.

By further condensation of the piperidone (VIII) with homoveratrylamine the diamide (XI) was obtained, which can also be prepared directly by the condensation of the methyl ester of β-(α'-cyano) propylglutaric acid with homoveratrylamine without isolation of the piperidone. The diamide was isolated as a thick yellow oil. By further cyclization with phosphorus oxychloride, the chloride of 4',5'-dimethoxy-6-ethyl-8-methyl-7-(1''-methyl-6'',7''-dimethoxy-3'',4''-dihydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenzo-(1',2':1,2)-quinolizine (XII) was obtained, which then was reduced in the presence of Raney nickel catalyst to 8-methylemetine (XIII). The base was isolated as a light yellow oil. By treatment of its ether solution with ether saturated with hydrogen chloride, the hydrochloride was obtained as a colorless, amorphous powder. We did not succeed in isolating the crystalline hydrochloride because of its very great solubility in alcohol.

The rubro-compound was not obtained by oxidation of the base 8-methylemetine (XIII) with bromine and iodine. Oxidation with bromine yielded a slightly yellowish substance, and on oxidation with iodine a yellow amorphous material was obtained. The ultraviolet spectra of these materials(Figure) greatly suggest the spectra of the salts of o-methylpsychotrine which, as is well known, is an intermediate product of the oxidation of emetine to rubroemetine.

Thus the presence of an alkyl substituent on carbon atom $C_8$ prevents the formation of the rubro-compound. This confirms the participation of carbon atom $C_8$ in the process of formation of rubroemetine from emetine.



Ultraviolet absorption spectra in alcohol: 1) products of oxidation of 8-methylemetine with iodine, 2) product of oxidation of 8-methylemetine with bromine.

## EXPERIMENTAL

Ethyl ester of α-methylacetonedicarboxylic acid(I). To sodium alcoholate prepared from 12.63 g of sodium and 267.5 ml of anhydrous ethyl alcohol were added 105.7 g of the ethyl ester of acetonedicarboxylic acid and 148.2 g of methyl iodide. The mixture was kept gently boiling for 3 hours. After cooling, the alcohol was distilled off in vacuo. To the residue was added 100 ml of water, and the oil that separated was extracted with benzene. The extract was dried with sodium sulfate. The benzene was distilled off and the residue was distilled. Yield 99.6 g (89%). The ethyl ester of α-methylacetonedicarboxylic acid was a colorless liquid, soluble in alcohol, ether, benzene, and chloroform, insoluble in water.

B. p. 118-119° (2 mm), $d^{20}_4$ 1.0914, $n^{20}D$ 1.4390, $MR_D$ 52.08; calculated 51.69 (for keto form), 52.74 (for enol form).

Found %: C 55.58, 55.40; H 7.67, 7.36. $C_{10}H_{16}O_5$. Calculated %: C 55.5; H 7.40.

Ethyl ester of α-methyl-β-hydroxyglutaric acid (II). 50 g of the ethyl ester of α-methylacetonedicarboxylic acid was hydrogenated in the presence of 3 g of Raney nickel catalyst at 140-150° and 100 atm for 4 hours. After the usual treatment the ethyl ester of α-methyl-β-hydroxyglutaric acid was isolated as a colorless liquid, readily soluble in organic solvents, insoluble in water. Yield 45.2 g (90.5%).

B. p. 115-116° (1.5 mm), $d^{20}_4$ 1.0778, $n^{20}D$ 1.4379, $MR_D$ 53.13; calculated 53.21.

Found %: C 55.71, 55.34; H 8.32, 8.19. $C_{10}H_{18}O_5$. Calculated %: C 55.45; H 8.25.

Ethyl ester of α-methyl-β-acetoxyglutaric acid (III). 36.5 g of the ethyl ester of α-methyl-β-hydroxyglutaric acid and 56 g of freshly distilled acetic anhydride were heated to gentle boiling for 1 hour. The excess acetic anhydride and acetic acid was distilled off in vacuo and the residue was distilled. The ethyl ester of α-methyl-β-acetoxyglutaric acid was a colorless liquid, soluble in alcohol, ether, benzene, and chloroform, insoluble in water. Yield 39.55 g (90.7%).

B. p. 124-125° (2 mm), $d^{20}_4$ 1.0772, $n^{20}D$ 1.4340, $MR_D$ 62.92; calculated 62.57.

Found %: C 55.58, 55.55; H 7.72, 7.58. $C_{12}H_{20}O_6$. Calculated %: C 55.53; H 7.74.

Ethyl ester of α-methylglutaric acid (IV). 32.53 g of the ethyl ester of α-methyl-β-acetoxyglutaric acid and 0.156 g of potassium acetate were heated so that acetic acid was distilled off but the temperature of the vapors did not exceed 140°. At the end of the distillation potassium acetate precipitated. Upon cooling the reaction mass was dissolved in ether and the ethereal solution was washed with water. When the acetic acid distillate was diluted with water, an additional amount of oil separated, which was extracted with ether and after being washed was added to the main extract. After the extract was dried with sodium sulfate, the ether was distilled off and the residue was distilled. Yield 25.5 g (88.4%). The ethyl ester of α-methylglutaric acid was a colorless liquid, soluble in the usual organic solvents, insoluble in water.

B. p. 104-105° (2 mm), $d^{20}_4$ 1.0475, $n^{20}D$ 1.4470; $MR_D$ 51.08; calculated 51.22.

Found %: C 60.25, 60.14; H 8.06, 7.83. $C_{10}H_{16}O_4$. Calculated %: C 60.00; H 8.00.

Ethyl ester of α-methyl-β-(cyano-carboethoxy)methylglutaric acid (V). A mixture of 25.5 g of the ethyl ester of α-methylglutaric acid, 29.2 g of ethyl cyanoacetate, and 20.4 ml of anhydrous ethyl alcohol was heated to gentle boiling for 12 hours. Every 2 hours 1/6 part of the sodium alcoholate prepared from 2.43 g of sodium and 27 ml of anhydrous ethyl alcohol was added. After the usual isolation process the ethyl ester of α-methyl-β-(cyano-carboethoxy)methylglutaric acid was obtained as a colorless liquid, soluble in the usual organic solvents, insoluble in water. Yield 21.5 g (58.8%).

B. p. 155-156° (1 mm), $d^{20}_4$ 1.1156, $n^{20}D$ 1.4570, $MR_D$ 76.45; calculated 76.25.

Found %: C 57.21, 57.67; H 7.35, 7.44. $C_{15}H_{23}O_6N$. Calculated %: C 57.5; H 7.35.

Ethyl ester of α-methyl-β-(α'-cyano-α'-carboethoxy)propylglutaric acid (VI). To a solution of sodium ethylate prepared from 3.11 g of sodium and 55.5 ml of anhydrous ethyl alcohol were added 35.5 g of the ethyl ester of α-methyl-β-(cyano-carboethoxy)methylglutaric acid and 40 g of ethyl iodide. The mixture was heated for 1 hour. The ethyl ester of α-methyl-β-(α'-cyano-α'-carboethoxy)propylglutaric acid was a colorless liquid, soluble in the usual organic solvents, insoluble in water. Yield 30 g (75.5%).

B. p. 158-159° (1 mm), $d^{20}_4$ 1.0904, $n^{20}D$ 1.4600, $MR_D$ 85.65; calculated 85.48.

Found %: C 59.80, 59.79; H 7.76, 7.74. $C_{17}H_{27}O_6N$. Calculated %: C 59.82; H 7.97.

Ethyl ester of α-methyl-β-(α'-cyano)propylglutaric acid (VII). To the sodium alcoholate prepared from 3.76 g of sodium and 105.1 ml of anhydrous ethyl alcohol were added 49.1 g of the ethyl ester of α-methyl-β-(α'-cyano-α'-carboethoxy)propylglutaric acid and 2.67 g of water and the mixture was allowed to stand for 12 hours. Then the reaction mass was heated for 1 hour. The excess alcohol was distilled off in vacuo. To the residue was added 50 ml of water and the solution was shaken several times with ether to remove the unsaponified ester. The water layer was acidified with concentrated hydrochloric acid to an acid reaction to Congo. The oil that separated was extracted with ether. The extract was dried with sodium sulfate. The ether was distilled off and the residue was heated at 180° for 40 minutes. Upon cooling it was dissolved in benzene and washed with an aqueous solution of sodium bicarbonate. After the benzene was distilled off, the residue was distilled. Yield 8.17g(24.4%, taking into account the unsaponified ester in the amount of 6.15 g).

The ethyl ester of α-methyl-β-(α'-cyano)propylglutaric acid was a thick, colorless liquid, soluble in the usual organic solvents, insoluble in water.

B. p. 130-132° (1 mm), $d^{20}_4$ 1.0754, $n^{20}D$ 1.4690, $MR_D$ 69.70; calculated 69.97.

Found %: C 62.2, 62.75; H 8.89, 8.79; N 5.44, 5.17. $C_{14}H_{23}O_4N$. Calculated %: C 62.43; H 8.63; N 5.24.

Ethyl ester of N-[β'-(3',4'-dimethoxyphenyl)ethyl]-β-methyl-δ-ethyl-α-piperidone-γ-acetic acid (VIII). 2.8 g of the ethyl ester of α-methyl-β-(α'-cyano)propylglutaric acid (VII) in 10 ml of anhydrous ethyl alcohol and 5 g of homoveratrylamine were hydrogenated in the presence of 3 g of Raney nickel catalyst at 90 atm and 110-115° for 2 hours. The catalyst was filtered off and the alcohol was distilled off in vacuo. The residue was dissolved in benzene and washed with 3% hydrochloric acid. The benzene was distilled off and the residue was distilled: 1st fraction b. p. 155-190° (0.15 mm), 0.6 g; 2nd fraction b. p. 203-204° (0.15 mm), 1.3 g (32%). Each fraction was redistilled: 1st fraction – unalkylated piperidone (0.45 g), b. p. 145-150° (0.1 mm); 2nd fraction – alkylated piperidone (0.57 g), b. p. 198-199° (0.1 mm).

Found %: C 67.17, 67.15; H 8.32, 8.49; N 3.91, 3.84. $C_{22}H_{33}O_5N$. Calculated %: C 67.49; H 8.5; N 3.58.

Ethyl ester of 4',5'-dimethoxy-6-ethyl-8-methyl-3,4,5,6,7,8-hexahydrobenzo-(1',2':1,2)-quinolizinyl-7-acetic acid (X). 0.35 g of N-alkylated piperidone, 5 ml of anhydrous toluene, and 4 ml of phosphorus oxychloride were heated for 1 hour to gentle boiling. The toluene and phosphorus oxychloride were distilled off in vacuo. The residue was washed with ether and dissolved in 5 ml of 6% hydrochloric acid. The solution was evaporated in vacuo. The chloride was dissolved in alcohol and treated with alcohol saturated with ammonia until the acid reaction to Congo disappeared. The precipitate of inorganic salts was removed. The filtrate was hydrogenated in the presence of Raney nickel catalyst at 70 atm and 75-80° for 2 hours. The catalyst was filtered off and the alcohol was distilled off in vacuo. The residue was dissolved in 5 ml of water and shaken with ether (twice with 5 ml). Then the aqueous solution was treated with ammonia, the oil that separated was extracted with ether, and the extract was dried with sodium sulfate. After the ether was distilled off, a light yellow oil remained. Yield 0.1 g (29.8%). The hydrochloride was obtained by treating an ethereal solution of the base with ether saturated with hydrogen chloride. It was a colorless, amorphous material, readily soluble in alcohol, acetone, and water, insoluble in ether; very hygroscopic. M. p. 126° (deformed at 65°). The hydrochloride was dissolved in 3% hydrochloric acid and the acid solution was evaporated in vacuo. The residue was dissolved in the minimum amount of alcohol and absolute ether was added until there was a slight turbidity. Upon prolonged standing, a white, crystalline precipitate separated out. Before analysis the material was dried for 1 hour at 1 mm and 110°. M. p. 184-185.5° (deformed at 180.5°).

Found %: C 64.05, 63.81; H 7.96, 8.23; N 3.61, 3.62. $C_{22}H_{34}O_4NCl$. Calculated %: C 64.2; H 8.33; N 3.4.

β''-(3'',4''-Dimethoxyphenyl)ethylamido-N-[β'-(3',4'-dimethoxyphenyl)-ethyl]-β-methyl-δ-ethyl-α-piperidone-γ-acetic acid (XI). 1.2 g of the ethyl ester of α-methyl-β-(α'-cyano)propylglutaric acid dissolved in 15 ml of anhydrous ethyl alcohol and 4.8 g of β-(3,4-dimethoxyphenyl)ethylamine were heated in an autoclave at a hydrogen pressure of 120 atm and 110-115° for 2 hours in the presence of Raney nickel catalyst. After cooling the catalyst was filtered out. The residue after distillation of the alcohol was heated on an oil bath at 180-190° for 3 hours. The cooled reaction mass was carefully washed with ether. The residue was dried in a vacuum desiccator. Yield 1.48 g (95.5 ). β''-(3'',4''-Dimethoxyphenyl)ethylamido-N-[β'-(3',4'-dimethoxyphenyl)ethyl]-β-methyl-δ-ethyl-α-piperidone-γ-acetic acid was a dark yellow, thick oil, soluble in alcohol and chloroform, insoluble in ether.

Found %: C 68.15, 68.29; H 7.94, 7.84; N 5.13, 5.26. $C_{30}H_{42}O_6N_2$. Calculated %: C 68.5; H 8.03; N 5.32.

8-Methylemetine (XIII). A mixture consisting of 1.48 g of β''-(3'',4''-dimethoxyphenyl)ethylamide of N-[β'-(3',4'-dimethoxyphenyl)ethyl]-β-methyl-δ-ethyl-α-piperidone-γ-acetic acid, 25 ml of toluene, and 12.84 ml of freshly distilled phosphorus oxychloride was heated to gentle boiling of the reaction mass for 1 hour. The excess phosphorus oxychloride and toluene was distilled off in vacuo. The residue was washed with absolute ether and dissolved in 10 ml of 6% hydrochloric acid. The solution was evaporated in vacuo to dryness. The residue was dissolved in alcohol and treated with alcohol saturated with ammonia until there was a slight alkaline reaction (to litmus). The precipitate of inorganic salts was removed. The filtrate was hydrogenated in the presence of Raney nickel catalyst at 125 atm and 75-80° for 2 hours. Upon cooling the catalyst was filtered out, the alcohol was distilled off in vacuo, and the residue was dissolved in 10 ml of water, shaken with ether several times, and then neutralized with ammonia. The oil that separated was extracted with ether. The extract was dried with potassium carbonate. After the solvent was distilled off, the base was isolated as a light yellow oil. Yield 0.4 g (28.9%). The hydrochloride was obtained by treating the ether solution of the base with ether saturated with dry hydrogen chloride. It was a colorless, amorphous material, readily soluble in alcohol, acetone, chloroform, and water, insoluble in ether. M. p. 121-122° (deforms at 73°).

Found %: N 4.76, 4.78. $C_{30}H_{42}O_4N_2 \cdot 2HCl$. Calculated %: N 4.93.

Oxidation of 8-methylemetine with bromine. To a solution of 0.18 g of the base 8-methylemetine in 0.36 ml of chloroform were gradually added 0.06 ml of bromine in 1.8 ml of chloroform. The reaction mass was kept at room temperature for 10 minutes, then treated with ammonia solution. After being dried the chloroform was distilled off, the residue was treated with water, the aqueous solution was evaporated in vacuo, and the residue was dissolved in alcohol. When absolute ether was added to the alcohol solution, a slightly yellow precipitate separated out, which was repeatedly washed and dried in a vacuum desiccator. M. p. 195-198° (deformed at 140°).

Found %: N 4.79, 4.96. $C_{30}H_{41}N_2Br$. Calculated %: N 4.85.

Oxidation of 8-methylemetine with iodine. A mixture consisting of 0.2 g of the base 8-methylemetine, 8 ml of anhydrous ethyl alcohol, and 0.4 g of iodine was heated to gentle boiling of the reaction mass for 3.5 hours. Upon cooling the alcohol solution was poured into a solution of sodium bicarbonate. The oily precipitate that formed was washed with sodium hydrosulfite and dissolved in acetone. After the acetone was evaporated in vacuo, the residue was dissolved in alcohol and reprecipitated with ether. M. p. 135-140° (deformed at 119°).

Found %: N 4.48, 4.70. $C_{30}H_{41}N_2I$. Calculated %: N 4.52.

$\lambda_{max}$ 225 mμ, lgε 4.41; λ 280 mμ, lgε 3.91; λ 310 mμ, lgε 3.71; λ 360 mμ, lgε 3.51; $\lambda_{min}$ 260 mμ, lgε 3.82; λ 295 mμ, lgε 3.69; λ 340 mμ, lg ε 3.44.

## SUMMARY

1. The synthesis of 8-methylemetine has been carried out.

2. It has been shown that the presence of a substituent on the carbon atom $C_8$ prevents the formation of a rubro-compound.

## LITERATURE CITED

[1] R. P. Evstigneeva, R. S. Livshits, L. I. Zakharkii, M. S. Bainova and N. A. Preobrazhenskii, Proc. Acad. Sci. USSR 75, 539 (1950); J. Gen. Chem. 22, 1467 (1952).*

[2] A. N. Dey, J. Chem. Soc. 1937, 1057.

[3] L. I. Zakharkii and N. A. Preobrazhenskii, J. Gen. Chem. 23, 518 (1953).*

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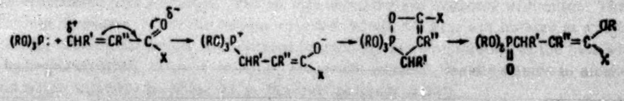
# ADDITION OF FULL ESTERS OF PHOSPHOROUS AND PHOSPHINOUS ACIDS TO CONJUGATED SYSTEMS

## V. THE PROBLEM OF THE MECHANISM OF THE REACTION OF TRIALKYL PHOSPHITES WITH CONJUGATED SYSTEMS

V. A. Kukhtin and Gil'm Kamai

In previous communications [1,2] we have described a new kind of Arbuzov rearrangement – the reaction of $C=C-C=O$ conjugated systems on esters of phosphorous and phosphinous acids. These reactions proceed according to the general scheme



The reaction mechanism proposed by us assumes preliminary partial ionization of the reacting molecules of the conjugated compound. In this connection it might be supposed that solvents promoting ionization would speed up the addition of phosphites to conjugated systems.

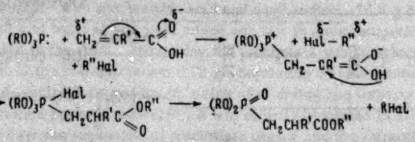
Experiments carried out by us to investigate the intensity of the addition reaction of tributyl phosphite to methacrylic acid in various solvents confirmed this assumption. We investigated the reaction of the above-mentioned reagents, taken in amounts of 0.1 g-mole in different solvents. 33.6 g of solvent was used, i.e., an amount equal to the sum of the starting reagents. All experiments were carried out at 50°. The course of the reaction was checked by the change in refractive index. The end of the reaction was determined by a constant refractive index and the absence of evolution of heat by a sample with $Cu_2Cl_2$. The completeness of the reaction was determined by distilling off the unreacted methacrylic acid. The data obtained are given in Table 1.

TABLE 1

| Solvent | Dielectric constant | Reaction time (in hours) | Percent conversion |
|---|---|---|---|
| Nitrobenzene | 36.4 | 6.5 | 88 |
| Acetone | 21.5 | 8.5 | 89.2 |
| Pyridine | 12.5 | 16.5 | 80 |
| Ether | 4.34 | 18 | 69 |
| Without solvent | – | 10.5 | 88.5 |

The experimental data show that the more polar the solvent, the more intensely the reaction proceeds; while solvents having a large dielectric constant speeded up the reaction, weakly polar solvents slowed it down in comparison to the case where the reaction was carried out without a solvent. The results obtained by us may serve to confirm the previously proposed reaction mechanism.

It also appeared to us very interesting to study the combined reaction of alkyl halides and unsaturated acids with trialkyl phosphites. Alkyl halides, as a rule, are less active in the Arbuzov rearrangement than α,β-unsaturated acids, which react with phosphites even at room temperature and in some cases with considerable evolution of heat. Therefore it might be assumed that in the first stage the phosphite would react predominantly with the α,β-unsaturated acid, and in the second stage, if the mechanism proposed by us corresponds to the actual course of the reaction, the alkyl halide would react actively with the bipolar ion formed or with the intermediate product and the reaction would go according to the scheme



The experiments carried out by us fully confirmed this assumption. Thus, for example, upon reaction of triethyl phosphite with acrylic acid and butyl bromide the butyl ester of β-(diethylphosphono)propionic acid was formed. Similarly, other phosphites, alkyl halides and acids also react in accordance with the above-presented scheme. In Table 3 are given the results of the experiments carried out by us. It is interesting to note that when ethyl bromide and methacrylic acid reacted with tributyl phosphite, in addition to the corresponding ester of β-phosphonoisobutyric acid there also were produced small amounts of butyl methacrylate. In other experiments, although we did not succeed in isolating the pure acrylates, their presence in the reaction products could be assumed because of their characteristic odor. The mechanism of their formation has still not been finally clarified by us.

TABLE 2

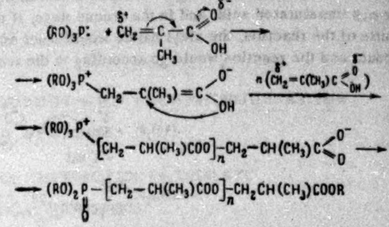
| Time (in hours) | $n^{20}_D$ | Increase in temperature with $Cu_2Cl_2$ | Time (in hours) | $n^{20}_D$ | Increase in temperature with $Cu_2Cl_2$ |
|---|---|---|---|---|---|
| 0 | 1.3938 | 11° | 4.5 | 1.3919 | 3.5° |
| 0.5 | 1.3938 | 11 | 5 | 1.3918 | 3.5 |
| 1 | 1.3935 | 10 | 5.5 | 1.3920 | 3 |
| 1.5 | 1.3938 | 11 | 6 | 1.3916 | 2.5 |
| 2 | 1.3934 | 8 | 6.5 | 1.3916 | 2.5 |
| 2.5 | 1.3931 | 7 | 7 | 1.3915 | 2 |
| 3 | 1.3928 | 6 | 7.5 | 1.3912 | 1 |
| 3.5 | 1.3923 | 5 | 8 | 1.3910 | 1 |
| 4 | 1.3921 | 4 | 8.5 | 1.3910 | 1 |

The results obtained by us confirm the correctness of the previously proposed mechanism for the reaction of trialkyl phosphites with C=C-C=O conjugated systems. The combined reaction of alkyl halides and α,β-unsaturated acids with phosphites also confirms the common reaction mechanism of the above-mentioned reagents with phosphites.

It also is interesting to note that when a reaction was carried out between triethyl phosphite, butyl iodide, and methacrylic acid at room temperature, we were not able to isolate the ester of phosphonoisobutyric acid. At the same time, in the course of the reaction a solid precipitate separated out, which after separation, careful washing, and drying formed a white, powdery, polymeric product at first taken by us to be a polymethacrylate. However, analysis showed that it contained 2.7% phosphorus, from which it was impossible to free it by purification. The formation of such a phosphorus-containing polymer, it seemed to us, might occur by telomerization of triethyl phosphite with methacrylic acid according to the scheme

TABLE 3

| Expt. no. | Starting reagents | Products isolated | Boiling point (pressure in mm) | $n_D^{20}$ | $d_0^{20}$ | % P found | % P calculated | Yield (in %) |
|---|---|---|---|---|---|---|---|---|
| 1 | 1) $CH_2=CHC\genfrac{}{}{0pt}{}{\nearrow O}{\searrow OH}$ | $(C_2H_5O)_2\underset{\underset{O}{\|}}{P}CH_2CH_2COOC_4H_9\text{-}n$ | 143—146° (8) | 1.4330 | 1.0549 | 11.66 | 11.65 | 17 |
| | 2) $n\text{-}C_4H_9Br$ | — | | | | | | |
| | 3) $(C_2H_5O)_3P$ | $C_2H_5Br$ | 38—40 | 1.4295 | — | — | — | 25.6 |
| 2 | 1) $CH_2=C(CH_3)C\genfrac{}{}{0pt}{}{\nearrow O}{\searrow OH}$ | $(n\text{-}C_4H_9O)_2\underset{\underset{O}{\|}}{P}CH_2\underset{\underset{CH_3}{\vert}}{CH}COOC_2H_5$ | 144—146 (3) | 1.4344 | 1.0418 | 10.2 | 10.05 | 21.3 |
| | 2) $C_2H_5Br$ | — | | | | | | |
| | 3) $(n\text{-}C_4H_9O)_3P$ | $CH_2=C(CH_3)COOC_4H_9\text{-}n$ | 68—70 (21) | 1.4280 | — | — | — | 10.4 |
| 3 | 1) $CH_2=\underset{\underset{CH_3}{\vert}}{C}-C\genfrac{}{}{0pt}{}{\nearrow O}{\searrow OH}$ | | | | | | | |
| | 2) $C_2H_5Cl$ | $(C_2H_5O)_2\underset{\underset{O}{\|}}{P}CH_2\underset{\underset{CH_3}{\vert}}{CH}COOC_2H_5$ | 146—148 (8) | 1.4314 | 1.0491 | 11.69 | 11.71 | 25.8 |
| | 3) $(C_2H_5O)_3P$ | — | | | | | | |



With a phosphorus content of 2.7% the polymer obtained should have a molecular weight of approximately 1150. The possibility of telomerization of trialkyl phosphites with methacrylic acid certainly is of great interest and needs further, more detailed investigation.

## EXPERIMENTAL

*Reaction of tributyl phosphite with methacrylic acid in acetone medium.* 25 g of phosphite, 8.5 g of methacrylic acid, and 33.6 g of acetone were heated in a small flask with a reflux condenser and a stirrer at 50°. Every 30 minutes the solution was quickly cooled to 20°, the refractive index was determined, and a test was made for the presence of phosphite with cuprous chloride (0.1 g of $Cu_2Cl_2$ per 0.2 g of reaction mixture). The results are given in Table 2.

In 8 hrs 30 min the reaction was considered practically completed, and after removal of the solvent the unreacted methacrylic acid was distilled off in vacuo. As a result of the distillation, 0.93 g of acid was isolated (10.8% of the initial amount).

The reaction was carried out in a similar manner in the other experiments. When pyridine was used as the solvent, tests were not made with $Cu_2Cl_2$, since pyridine reacts with cuprous halide. The yield of the butyl ester of β-phosphonoisobutyric acid was in all cases 40-50%.

*Reaction of triethyl phosphite with acrylic acid and butyl bromide.* To 20 g of triethyl phosphite and 16.6 g of butyl bromide was added dropwise 8.7 g of acrylic acid. Some time after the beginning of the addition the temperature of the reaction mass started to rise and gradually reached 65-70°. After the evolution of heat ended, the reaction mass was heated on a water bath for 2 hours. As a result of repeated fractionation 5.4 g of the butyl ester of β-(diethylphosphono)propionic acid was isolated.

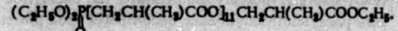
B. p. 143-146° (8 mm), $n^{20}D$ 1.4330, $d^{20}_4$ 1.0549, $MR_D$ 62.16; calculated 65.51.

Found %: P 11.69. $C_{11}H_{23}O_5P$. Calculated %: P 11.71.

The remaining experiments were carried out in a similar manner (Table 3).

Reaction of triethyl phosphite with methacrylic acid and butyl iodide. 16.6 g of triethyl phosphite, 8.6 g of methacrylic acid, and 18.3 g of butyl iodide were mixed and left at room temperature. In several hours a flocculent precipitate appeared in the flask. After a day the precipitate was separated, carefully washed with ether, and dried. The weight of the precipitate was 0.78 g. Separation of precipitate continued on the second and third day. In all 2.1 g of precipitate was formed, which after drying and washing was a white powder that did not melt, but gradually turned brown at 200-210°. It was difficultly soluble in acetone, but dissolved readily in alkalized water. In three days the separation of precipitate ceased and the refractive index of the reaction mixture did not change further. It was not possible to isolate individual compounds by fractional distillation of the liquid portion of the reaction products.

Found %: P 2.71; C 53.9; H 7.49. M(Rast method) 1190.



$(C_2H_5O)_2\underset{O}{\underset{\|}{P}}[CH_2CH(CH_3)COO]_{11}CH_2CH(CH_3)COOC_4H_9$. Calculated %: P 2.59; C 54.1; H 7.31. M 1198.

## SUMMARY

1. The effect of solvents on the reaction of tributyl phosphite with methacrylic acid has been investigated. It has been established that polar solvents accelerate this reaction.

2. Combined reactions of trialkyl phosphites with α, β-unsaturated acids and alkyl halides have been investigated. The products of their joint reaction have been isolated and a reaction mechanism has been proposed.

## LITERATURE CITED

[1] Gil'm Kamai and V. A. Kukhtin, Proc. Acad. Sci. USSR 109, 91 (1956);* J. Gen. Chem. 27, 2376 (1957).*

[2] Gil'm Kamai and V. A. Kukhtin, Trans. KKhTI No. 23, 133 (1957).

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* Original Russian pagination. See C. B. Translation.

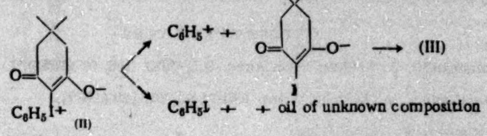
# IODONIUM DERIVATIVES OF β-DIKETONES

## II. THERMAL DECOMPOSITION OF PHENYLDIMEDONYLIODONE

O. Ia. Neiland, G. Ia. Vanag and E. Iu. Gudrinietse

We have shown [1] that dimedon (5,5-dimethylcyclohexanedione-1,3) (I) reacts very readily with iodosobenzene, forming an iodonium derivative of the enol-betaine type – phenyldimedonyliodone (II). The product after recrystallization and drying in vacuo was completely stable at ordinary temperature, but unpurified phenyldimedonyliodone gradually decomposed in storage. Pure phenyldimedonyliodone decomposes upon prolonged boiling of its aqueous solutions and also when it is boiled in toluene or heated without a solvent above the melting point (139°). It was possible to isolate from the decomposition products iodobenzene and the phenyl ether of iododimedon (III), the composition of which was demonstrated by splitting it with acids to the phenol and converting to the phenyl ether of dimedon (IV). The latter was smoothly split by acids to phenol and dimedon.

The decomposition of phenyldimedonyliodone can be represented by the following diagram.



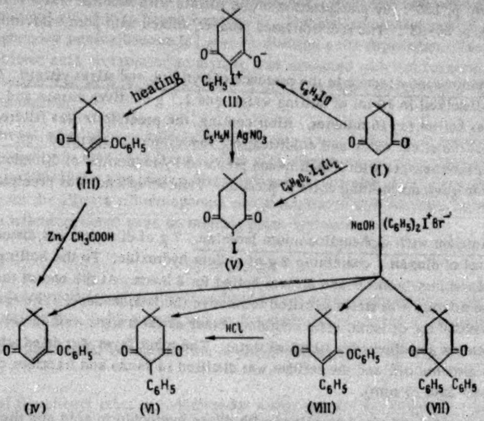
Depending on the place of rupture of the C–I bond, either the phenyl ether of iododimedon or iodobenzene is obtained.

The proposed mechanism for the decomposition of phenyldimedonyliodone is in complete agreement with the already known mechanisms for the decomposition of iodonium salts [2-4].

$$[Ar—I—Ar]^+ + X^- \rightarrow ArI + ArX$$

The decomposition of phenyldimedonyliodone in the presence of pyridine and silver nitrate yielded the silver salt of iododimedon (V), which confirms the suggested scheme for the decomposition with initial formation of an iododimedon anion and a phenyl cation. The formation of N-phenylpyridinium could be demonstrated but considerable amounts of phenol were found. Investigation of the decomposition of phenyldimedonyliodone clearly showed that this compound has an iodonium salt structure.

Phenyl ethers of dimedon have not been described in the literature up to the present time. We attempted to prepare the phenyl ether of dimedon (IV) in another way also – by direct phenylation of dimedon with diphenyliodonium bromide. Although similar reactions are described in the literature [5], they have not been used for the phenylation of β-diketones. We succeeded in isolating all four theoretically possible products – the phenyl ether of dimedon (IV), phenyldimedon (VI), diphenyldimedon (VII), and the phenyl ether of phenyldimedon (VIII), but in small yields (8-18%). The phenyl ether of dimedon (IV) was isolated in insignificant amounts, because it was difficult to purify; however, no depression was observed in a mixed melting point test with previously prepared material, which permits considering them identical. The structure of diphenyldimedon (VII) was demonstrated by sodium hydroxide fusion. Diphenylmethane and β,β-dimethylglutaric acid were produced. The phenyl ether of phenyldimedon (VIII) was split by the action of acid to phenol and phenyldimedon (VI) (see diagram).



The phenylation reaction of dimedon that was investigated proceeded rapidly and could be used for the preparation of difficultly available phenyl derivatives of dimedon.

## EXPERIMENTAL

Phenyl ether of iododimedon (III). 34.2 g of phenyldimedonyliodone (II) was boiled for 1 hour with 300 ml of toluene. The reaction mixture was distilled in vacuo and an iodobenzene fraction was collected with b. p. 63-64° (8 mm), 8.2 g (40%). The residue was washed with 2N potassium hydroxide solution and dried at 100°. Yield 16 g (47%). M. p. 158-162°. The phenyl ether of iododimedon crystallized from glacial acetic acid as yellowish prisms. M. p. 165-166°.

Found %: I 36.98, 37.33. $C_{14}H_{15}O_2I$. Calculated %: I 37.13.

Oxime of the phenyl ether of iododimedon. 0.1 g of the phenyl ether of iododimedon was boiled with 0.4 g of hydroxylamine hydrochloride in 3 ml of pyridine for 2 hours. After dilution with water 0.12 g of precipitate was obtained. It was crystallized from 5 ml of alcohol. Colorless, small needles. M. p. 210° (decomp.).

Found %: N 3.71. $C_{14}H_{16}O_2NI$. Calculated %: N 3.92.

Splitting of the phenyl ether of iododimedon with sulfuric acid. 0.684 g of the phenyl ether of iododimedon was boiled with 10 ml of 50% alcohol and 3 drops of concentrated sulfuric acid for 2 hours. The mixture was diluted with 10 ml of water, filtered off from the tarry materials, and precipitated with bromine water. Yield 0.6 g (91%). The tribromophenol obtained was crystallized from aqueous alcohol. A mixed sample with pure tribromophenol gave no depression in melting point.

Phenyl ether of dimedon (IV). 3.42 g of the phenyl ether of iododimedon (III) was boiled for 2 hours with 35 ml of glacial acetic acid while 15 g of zinc dust was gradually added. The mixture was filtered and diluted with 5 times its amount of water. An emulsion was obtained that slowly started to crystallize. Yield 1.4 g (65%). M. p. 78-80°, b. p. 154-156° (7 mm). After distillation the m. p. was 80-82°. The phenyl ether of dimedon was a white crystalline material, readily soluble in all organic solvents.

Found %: C 77.57; H 7.60. $C_{14}H_{16}O_2$. Calculated %: C 77.78; H 7.41.

Splitting of the phenyl ether of dimedon with hydrochloric acid. 0.108 g of the phenyl ether of dimedon was boiled with 1 ml of alcohol, 2 ml of water, and 0.3 ml of concentrated hydrochloric acid for 45 minutes. The mixture was diluted with water and several drops of formalin added and it was heated to boiling. Upon cooling, formaldodimedon (methylenebisdimedon) separated. Yield 0.04 g (60%). After crystallization from alcohol the m. p. was 188°. A mixed sample with a pure preparation gave no depression in melting point. According to data in [6], m. p. 189°. By precipitation of the filtrate with bromine water 0.15 g of tribromophenol (90%) was obtained. M. p. 80-83°. The recrystallized product, mixed with pure tribromophenol, gave no melting point depression.

Splitting of phenyldimedonyliodone in the presence of pyridine and silver nitrate. 0.9 g of phenyldimedonyliodone hydrate was dissolved in 10 ml of boiling water, and 1.7 g of silver nitrate and 1 ml of pyridine were added. The mixture was boiled for 15 minutes. After cooling, the precipitate was filtered off and treated with alkali. After removal of the silver oxide and acidification, iododimedon separated out. Yield 0.5 g (75%). M. p. 165° (decomp.). A mixed sample with iododimedon prepared by iodination of dimedon by a complex of iodine chloride with dioxan gave no melting point depression. Tribromophenol was precipitated from the filtrate with bromine water.

Phenylation of dimedon with diphenyliodonium bromide. 7 g of dimedon was dissolved in a mixture of 30 ml of water and 30 ml of dioxan, containing 2 g of sodium hydroxide. To the boiling mixture was gradually added 18 g of diphenyliodonium bromide and all was boiled for 2 hours. At the end of the reaction a layer of yellow oil formed. The mixture was steam distilled to remove the iodobenzene. The residue was treated first with 70 ml, and then with 30 ml of ether. The combined ether extracts were washed twice with 20 ml of 10% potassium carbonate solution and then with 10 ml of water. The ether layer was dried with anhydrous calcium chloride, the ether was distilled off, and the residue was distilled in vacuo and fractions collected with b. p. 150-160° (7 mm) and 160-210° (7 mm).

a) The alkali layer obtained was neutralized with dilute hydrochloric acid and the precipitate was washed with 30 ml of ether and crystallized from 10 ml of alcohol and 20 ml of water. Phenyldimedon (VI) crystallized as lustrous leaflets. Yield 0.92 g (8.5%). M. p. 192-193°.

Found %: C 77.21; H 7.39. $C_{14}H_{16}O_2$. Calculated %: C 77.78; H 7.41.

b) The fraction with b. p. 150-160° (7 mm) was a colorless oil that slowly crystallized. The crystals that formed were pressed out on filter paper, ground to a powder, and dried in vacuo. They were recrystallized from dilute acetic acid. The phenyl ether of dimedon (IV) obtained crystallized as flat prisms. Insignificant yield. M. p. 70-75°. A mixture with the phenyl ether of dimedon prepared from phenyldimedonyliodone melted at 70-78°.

c) The fraction with b. p. 160-210° (7 mm) was a yellow, viscous oil, which was treated with 6 ml of alcohol. The insoluble residue was filtered and washed with alcohol. Yield of diphenyldimedon (VII) 0.6 g (8.2%). M. p. 175-176°. From alcohol – white, flat needles.

Found %: C 81.87; H 6.94. $C_{20}H_{20}O_2$. Calculated %: C 82.19; H 6.85.

d) The alcohol solution (see b) obtained was evaporated. Crystals slowly separated out from the yellow mass and solidified in a week. Yield 1.3 g (17.8%). M. p. 50-60°. The mass was dissolved in glacial acetic acid and precipitated with water. The semicrystalline paste was pressed out on filter paper and recrystallized repeatedly from dilute acetic acid. The phenyl ether of phenyldimedon (VIII) that was obtained formed small prisms. M. p. 85-87°.

Found %: C 81.66; H 7.21. $C_{20}H_{20}O_2$. Calculated %: C 82.19; H 6.85.

2-Nitro-2-phenyldimedon. To a suspension of phenyldimedon (VI) in ether was added several drops of fuming nitric acid until solution was complete. The ethereal solution was washed with water and evaporated. The nitrophenyldimedon crystallized from alcohol as leaflets. M. p. 163-164° (decomp.).

Found %: N 5.56. $C_{14}H_{15}O_4N$. Calculated %: N 5.36.

2-Iodo-2-phenyldimedon. 0.11 g of phenyldimedon (VI) and 0.2 g of a complex of iodine chloride and dioxan were dissolved in 2 ml of glacial acetic acid. Upon dilution of the solution with water 0.14 g (40%) of iodo-phenyldimedon precipitated. M. p. 85-87°. The compound crystallized from alcohol as yellow, flat needles. M. p. 89-91°.

Found % I 37.45. $C_{14}H_{15}O_2I$. Calculated % I 37.13.

Splitting of diphenyldimedon (VII). A small amount of diphenyldimedon was fused with sodium hydroxide. An oil separated with an odor of mandarin peel – diphenylmethane, which was extracted with carbon tetrachloride and oxidized with chromyl chloride to benzophenone [7]. The semicarbazone melted at 163-164°. A mixed sample with pure benzophenone semicarbazone [8] gave no melting point depression. The alkaline mass was neutralized with hydrochloric acid, evaporated to dryness, and extracted with hot benzene. Upon cooling, β,β-dimethylglutaric acid crystallized with m. p. 100-102°. A mixed sample with pure β,β-dimethylglutaric acid gave no melting point depression.

Splitting of the phenyl ether of phenyldimedon (VIII). An alcohol solution of compound (VIII) was boiled with several drops of hydrochloric acid for 2 hours. When diluted with water, phenyldimedon (VI) separated out as lustrous leaflets. M. p. 188-190°. The recrystallized product mixed with pure phenyldimedon gave no melting point depression. From the filtrate tribromophenol was precipitated with bromine water. M. p. 85-88°. A mixed sample with pure tribromophenol gave no melting point depression.

## SUMMARY

1. Upon thermal decomposition of phenyldimedonyliodone a new compound was formed – the phenyl ether of iododimedon; besides this, iodobenzene and an oily material of unknown composition are obtained.

2. The products of the thermal decomposition of phenyldimedonyliodone confirmed its iodonium structure.

3. By reduction of the phenyl ether of iododimedon a new product was obtained – the phenyl ether of dimedon.

4. By direct phenylation of dimedon with diphenyliodonium bromide new products were obtained – the phenyl ether of dimedon, phenyldimedon, diphenyldimedon, and the phenyl ether of phenyldimedon.

## LITERATURE CITED

[1] E. Iu. Gudrinietse, O. Ia. Neiland, and G. Ia. Vanag, J. Gen. Chem. 27, 2737 (1957).*

[2] H. J. Lucas, E. R. Kennedy, C. A. Wilmot, J. Am. Chem. Soc. 58, 157 (1936).

[3] R. B. Sandin, M. Kulka, R. McCready, J. Am. Chem. Soc. 59, 2014 (1937).

[4] L. G. Makarova and A. N. Nesmeianov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1945, 617.

[5] F. M. Beringer, M. Drexler, E. M. Gindler, Ch. C. Lumpkin, J. Am. Chem. Soc. 75, 2718 (1953).

[6] D. Vorländer, A. Erig, Lieb. Ann. 294, 316 (1897).

[7] G. Law, F. Perkin, J. Chem. Soc. 93, 1637 (1902).

[8] A. Borsche, G. Merkwitz, Ber. 37, 3180 (1904).

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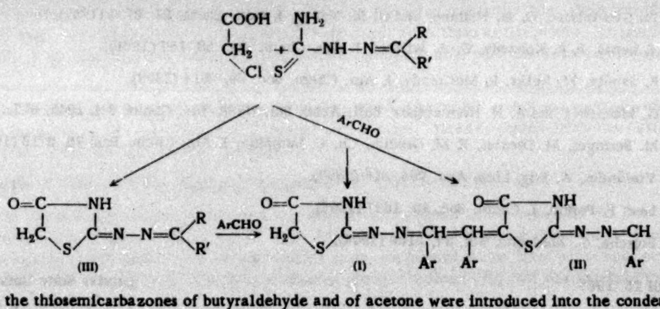
* Original Russian pagination. See C. B. Translation.

# SYNTHESIS OF THIAZOLIDONE DERIVATIVES HAVING BIOLOGICAL INTEREST

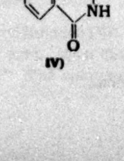
## VIII. REPLACEMENT OF SOME RADICALS OF OXO-COMPOUNDS BY OTHERS IN THE MOLECULES OF DERIVATIVES OF THIAZOLIDINEDIONE-2,4-HYDRAZONE-2

N. M. Turkevich and E. V. Vladzimirskaia

In previous communications [1-3] we described for the first time the synthesis of 5-arylidene monoderivatives and 5-arylidene bisderivatives of thiazolidinedione-2,4-arylidenehydrazones-2. In that work we made attempts to prepare analogous derivatives of thiazolidinedione-2,4-alkylidenehydrazones-2, which led to the establishment of new rules for the synthesis of thiazolidine derivatives. It appeared that when the thiosemicarbazones of oxo-compounds of the aliphatic and hydroaromatic series are heated with monochloroacetic acid in the presence of aromatic aldehydes, the expected 5-arylidene derivatives are not formed, but the substitution of the oxo-compounds mentioned by arylidene groups ensues (see diagram). As a result, various 2''-arylidene derivatives of thiazolidinedione-2,4-hydrazone-2 (I) were obtained, which are presented by us in Table 1. As concerns the thiosemicarbazones of the oxo-compounds of the aromatic series, we observed the replacement of some of the arylidene groups by others only in the case of heating of a mixture of the thiosemicarbazone of p-isopropylbenzaldehyde with monochloroacetic acid and p-nitrobenzaldehyde, whereupon thiazolidinedione-2,4-p-nitrobenzylidenehydrazone-2 was obtained (see Table 1).



When the thiosemicarbazones of butyraldehyde and of acetone were introduced into the condensation reaction with monochloroacetic acid in the presence of benzaldehyde, we observed the formation of the 5,2''-dibenzylidene derivative (II, Ar=$C_6H_5$). The identical compound was synthesized by us [3] by the condensation of thiosemicarbazide with monochloroacetic acid in the presence of an excess of benzaldehyde.



(IV)

TABLE 1

| Expt. no. | Thiosemicarbazone | Aromatic aldehyde | Condensation product | Melting point | Yield (in %) | Analysis for N (in %) | |
|---|---|---|---|---|---|---|---|
| | | | | | | found | calc. |
| 1 | Glucose | Benzaldehyde | (I), $Ar{=}C_6H_5$ | 257—258° | 55 | 19.54 | 19.17 |
| 2 | Menthone | Benzaldehyde | (I), $Ar{=}C_6H_5$ | 259 | 87.5 | 19.19 | 19.17 |
| 3 | Cyclohexanone | Benzaldehyde | (I), $Ar{=}C_6H_5$ | 252 | 76 | 18.78 | 19.17 |
| 4 | Glucose | Anisaldehyde | (I), $Ar{=}p\text{-}CH_3OC_6H_4$ | 254—255 | 64.5 | 16.90 | 16.86 |
| 5 | Glucose | Salicylaldehyde | (I), $Ar{=}o\text{-}HOC_6H_4$ | $>300$ | 89.5 | 17.88 | 17.86 |
| 6 | Menthone | Salicylaldehyde | (I), $Ar{=}o\text{-}HOC_6H_4$ | $>300$ | 95 | 17.82 | 17.86 |
| 7 | Chloral | Salicylaldehyde | (I), $Ar{=}o\text{-}HOC_6H_4$ | $>300$ | 70.5 | 18.01 | 17.86 |
| 8 | Glucose | m-Nitrobenzaldehyde | (I), $Ar{=}m\text{-}O_2NC_6H_4$ | 270 | 72 | 21.05 | 21.20 |
| 9 | Chloral | m-Nitrobenzaldehyde | (I), $Ar{=}m\text{-}O_2NC_6H_4$ | 272 | 69 | 21.15 | 21.20 |
| 10 | Glucose | o-Chlorobenzaldehyde | (I), $Ar{=}o\,ClC_6H_4$ | 255 | 88.5 | 16.58 | 16.56 |
| 11 | Menthone | o-Chlorobenzaldehyde | (I), $Ar{=}o\text{-}ClC_6H_4$ | 255 | 95 | 16.60 | 16.56 |
| 12 | Cuminal | p-Nitrobenzaldehyde | (I), $Ar{=}p\text{-}O_2NC_6H_1$ | 270 | 98 | 21.26 | 21.20 |
| 13 | Butyraldehyde | Benzaldehyde | (II), $Ar{=}C_6H_5$ | 283 | 47 | 13.72 | 13.60 |
| 14 | Acetone | Benzaldehyde | (II), $Ar{=}C_6H_5$ | 283 | 40 | 13.90 | 13.60 |
| 15 | Acetone | Aldehydophthalic acid | (IV) | 185 | 82 | 19.32 | 19.17 |

The condensation of the thiosemicarbazone of acetone with monochloroacetic acid in the presence of aldehydophthalic acid led to the formation of phthalazone (IV) which gave no depression with a preparation obtained by the method of Gabriel et al.[4].

Replacement of some groups of oxo-compounds by others was observed by us not only upon condensation of monochloroacetic acid with thiosemicarbazones in the presence of aromatic aldehydes, but also upon reaction of aromatic aldehydes with prepared aliphatic and hydroaromatic derivatives of thiazolidinedione-2,4-hydrazone-2 (III), which were synthesized by us by the method of Chabrier et al [5] (see diagram). The results of the pertinent studies are presented in Table 2.

For the identification of the condensation products obtained we synthesized various thiazolidinedione-2,4-arylidenehydrazones-2 [5]. Of these, the 2''-o-chlorobenzylidene- and 2''-m-nitrobenzylidene derivatives have not been described in the literature up to the present time. In all cases a mixed melting point test of the same condensation products prepared by the various methods did not give any depression. Because of the fact that the reaction products with salicylaldehyde (see Table 1 and 2) melt above 300°, their identification was carried out by means of the ultraviolet absorption spectra. The results of the investigations showed that the preparations referred to were identical with respect to absorption maxima and intensities with thiazolidinedione-2,4-salicylidenehydrazone-2 prepared by the method of Chabrier et al.(after 3 recrystallizations from glacial acetic acid the preparation did not melt, as Chabrier indicates, at 255°, but its melting point was above 300° [3]).

## EXPERIMENTAL

Equimolecular amounts (12.5 millimoles) of thiosemicarbazone, aromatic aldehyde, and monochloroacetic acid were refluxed in 50-80 ml of glacial acetic acid for 1-2 hours. After the reaction mixture was diluted with a saturated solution of $CH_3COONa$, the condensation product was filtered off and recrystallized from acetic acid, with the exception of phthalazone, which was recrystallized from water. In the case of the use of the thiosemicarbazones of glucose and chloral for the condensation, the reaction was carried out for 6 hours in alcohol.

We obtained the hydrate of the thiosemicarbazone of chloral first in 77.5% yield by mixing a hot solution of 0.1 g of thiosemicarbazide in 25 ml of water with a cold solution of 16.6 g of chloral hydrate in 20 ml of

TABLE 2

| Experiment No. | Substituent in position 2' of init. prod. (III) | Aromatic aldehyde | Condensation product | Melting point | Yield (in %) | Analysis for N (in %) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Found | Calculated |
| 1 | Isopropylidene | Benzaldehyde | (I), $Ar=C_6H_5$ | 257° | 62 | 19.12 | 19.17 |
| 2 | Cyclohexylidene | p-Anisaldehyde | (I), $Ar=p\text{-}CH_3OC_6H_4$ | 255 | 66 | 16.92 | 16.86 |
| 3 | n-Butylidene | Salicylaldehyde | (I), $Ar=o\text{-}HOC_6H_4$ | >300 | 66 | 17.70 | 17.86 |

water, with subsequent shaking of the mixture until it cooled. The precipitate was filtered off and recrystallized from water. M. p. 90° (decomp.).

Found %: N 17.62, 17.51. $C_3H_6ON_3SCl_3$. Calculated %: N 17.62.

The replacement of some of the groups of the oxo-compounds by others from prepared derivatives of thiazolidinedione-2,4-hydrazone-2 was carried out by refluxing 20 millimoles of the starting material (see Table 2), 16 millimoles of the aromatic aldehyde, and 16 ml of glacial acetic acid for 1 hour. From the solution formed at first the reaction product separated out after some time as a precipitate which was filtered off, washed with water, and recrystallized from acetic acid.

## SUMMARY

1. By the condensation of thiosemicarbazones of the aliphatic or hydroaromatic series with monochloroacetic acid in the presence of aromatic aldehydes, 2''-monoarylidene- or 2'',5-diarylidene derivatives of thiazolidinedione-2,4-hydrazone-2 are produced.

2. Upon the reaction of derivatives of thiazolidinedione-2,4-hydrazone-2 of the aliphatic or hydroaromatic series with aromatic aldehydes, the replacement of some groups of the oxo-compounds by others is observed.

## LITERATURE CITED

[1] E. V. Vladzimirskaia and N. M. Turkevich, J. Gen. Chem. 25, 2150 (1955).*

[2] E. V. Vladzimirskaia, J. Gen. Chem. 27, 1345 (1957).*

[3] E. V. Vladzimirskaia, J. Gen. Chem. 27, 2898 (1957).*

[4] S. Gabriel, A. Neumann, Ber. 26, 523 (1893).

[5] P. Chabrier, E. Cattelain, Bull. Soc. Chim. (5) 17, 48 (1950).

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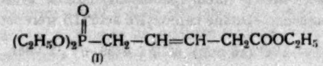
* Original Russian pagination. See C. B. Translation.

# A NEW METHOD OF SYNTHESIZING ESTERS OF PHOSPHINIC AND THIOPHOSPHINIC ACIDS

## XXIX. THE ADDITION OF DIALKYL PHOSPHOROUS ACIDS TO ESTERS OF VINYLACRYLIC AND SORBIC ACIDS AND 3,5 HEPTADIENE-2-ONE

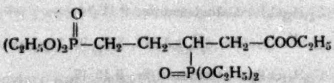
A. N. Pudovik and I. V. Konovalova

As we previously showed, the addition of dialkyl phosphorous acids to esters of $\alpha,\beta$-unsaturated carboxylic acids and $\alpha,\beta$-unsaturated ketones leads to the formation of esters of phosphone carboxylic acids and phosphone ketones [1]. The reactions with dialkyl thiophosphorous acids and acid esters of alkyl and aryl phosphinic acids [2] proceed in a similar manner. The present paper describes the results of an investigation of the addition reactions between dimethyl phosphorous and diethyl phosphorous acids and the ethyl esters of $\beta$-vinylacrylic and sorbic acids, 3,5-heptadiene-2-one and the diethyl ester of butadiene phosphinic acid. Alcoholates of the alkali metals were used as catalysts in these reactions. All the reactions take place very vigorously and are accompanied by a considerable thermal effect. As a result of the addition of diethyl phosphorous acid (in excess) to the ethyl ester of $\beta$-vinylacrylic acid addition products of one and two acid molecules were obtained, i.e., the ethyl esters of 4-(diethylphosphone)butene-2-carboxylic acid (I) and 2,4-di-(diethylphosphone) butane carboxylic acid (II).



$(C_2H_5O)_2\overset{\overset{\displaystyle O}{\|}}{P}-CH_2-CH=CH-CH_2COOC_2H_5$

(I)

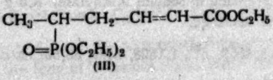


$(C_2H_5O)_2\overset{\overset{\displaystyle O}{\|}}{P}-CH_2-CH_2-\underset{\underset{\displaystyle O=P(OC_2H_5)_2}{|}}{CH}-CH_2-COOC_2H_5$

(II)

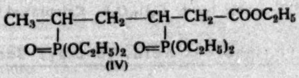
The structure of (I) was proven by ozonization. Acetaldehyde was identified in the form of the condensation product with dimedone. Formaldehyde was not found. Acetaldehyde can obviously be formed only from the ester of formylacetic acid as a result of its saponification and decarboxylation, which take place under the conditions of decomposition of ozonides (heating with water).

The addition of diethyl phosphorous acid to the ethyl ester of sorbic acid also leads to the formation of two products (III) and (IV).



$CH_3-\underset{\underset{\displaystyle O=P(OC_2H_5)_2}{|}}{CH}-CH_2-CH=CH-COOC_2H_5$

(III)



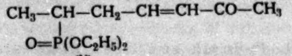
$CH_3-\underset{\underset{\displaystyle O=P(OC_2H_5)_2}{|}}{CH}-CH_2-\underset{\underset{\displaystyle O=P(OC_2H_5)_2}{|}}{CH}-CH_2-COOC_2H_5$

(IV)

The substance (III) contains only one double bond and is the addition product of one molecule of diethyl phosphorous acid. After its ozonization ethyl glyoxylate and acetaldehyde were identified in the form of condensation products with dimedone. Only a small amount of acetaldehyde was found. Acetaldehyde can evidently be formed directly from the ozonide of the α,β-addition product or from the ester of formylacetic acid, as indicated above, in the case of the presence of the α,δ-addition product. The conclusion may, therefore, be drawn from the results obtained that (III) is mainly a γ,δ-addition product containing α,β- or α,δ-forms or both together. The presence of the ester of formylacetic acid in its enol form in the decomposition products of ozonides was qualitatively confirmed by the reaction with ferric chloride.

(IV) does not contain a double bond and is the addition product of two molecules of diethyl phosphorous acid and ethyl sorbate, the ethyl ester of 2,4-di-(diethylphosphone) pentacarboxylic acid.

As a result of the addition of diethyl phosphorous acid and 3,5-heptadiene-2-one an addition product (V), containing one double bond, was obtained.



$$\underset{O=P(OC_2H_5)_2}{CH_3-\overset{}{CH}}-CH_2-CH=CH-CO-CH_3$$

(V)

After the ozonization of (V) methyl glyoxal was identified in the form of its dimedone derivative; from this the conclusion may be drawn that (V) is 6-(diethylphosphone)-3-heptene-2-one. Similar results were also obtained with dimethyl phosphorous acid. In conclusion, we carried out the addition of diethyl phosphorous acid and the ethyl ester of butadiene phosphinic acid. A 48% yield of the reaction product, di-(diethylphosphone)-butene, was obtained. The position of the double bond in it was not established.

## EXPERIMENTAL

### The Addition of Dialkyl Phosphorous Acids to Ethyl β-Vinylacrylate

1. The addition of diethyl phosphorous acid. An alcoholic solution of sodium ethylate was added gradually to the reaction mixture consisting of 19 g of diethyl phosphorous acid and 16.2 g of β-vinylacrylic acid (a slight excess of diethyl phosphorous acid was used). The reaction proceeded extremely vigorously and the flask was cooled with water. 10.5 g of the ethyl ester of (diethylphosphone)-butene-2-carboxylic acid (I) and 13.5 g of the ethyl ester of 2,4-di-(diethylphosphone)-butane carboxylic acid (II) were obtained by distillation.

(I) B. p. 167-168° (10 mm), 174-176° (18 mm), $n^{20}$D 1.4489, $d^{20}_4$ 1.0851, MR$_D$ 65.15; calculated 65.04.

Found %: P 11.91, 11.99. $C_{11}H_{21}O_5P$. Calculated %: P 11.74.

(II) B. p. 235-237° (12 mm), $n^{20}$D 1.4510, $d^{20}_4$ 1.1262, MR$_D$ 96.16; calculated 96.57.

Found %: P 15.18, 15.13. $C_{15}H_{32}O_8P_2$. Calculated %: P 15.42.

Ozonization. Ozonized oxygen was passed through a solution of 5.5 g of the ethyl ester of 4-(diethylphosphone)-butene-2-carboxylic acid in 22 ml of carbon tetrachloride for 24 hours. After the distillation of the carbon tetrachloride the ozonide was decomposed by heating with water. The volatile decomposition products were trapped in a 50% aqueous-alcoholic solution of dimedone. After recrystallization the white crystalline precipitate had an m. p. of 142°. A mixed melt of this substance and the condensation product of acetaldehyde and dimedone showed no depression of the melting point.

2. The addition of dimethyl phosphorous acid. The reaction was carried out with 4.4 g of dimethyl phosphorous acid and 5 g of ester in the presence of sodium methylate. 3.5 g of the ethyl ester of 4-(dimethylphosphone)-butene-2-carboxylic acid was obtained.

B. p. 172-173° (11 mm), $n^{20}$D 1.4552, $d^{20}_4$ 1.1528, MR$_D$ 55.58; calculated 55.81.

Found %: P 12.70, 13.22. 87% double bond. $C_9H_{17}O_5P$. Calculated %: P 13.13.

### The Addition of Dialkyl Phosphorous Acids to Ethyl Sorbate

1. The addition of diethylphosphorous acid. The reaction was carried out with 19 g of diethyl phosphorous

acid and 19 g of ethyl sorbate in the presence of sodium ethylate and was accompanied by a considerable liberation of heat. As a result of distillation 16.5 g of the ethyl ester of (diethylphosphone)-pentene carboxylic acid (III) and 11 g of the ethyl ester of 2,4-di-(diethylphosphone)-pentene carboxylic acid (IV) were obtained.

(III) B. p. 165-166° (10 mm), $n^{20}D$ 1.4500, $d^{20}_4$ 1.0638, $MR_D$ 70.25; calculated 69.67.

Found %: P 10.97, 11.03. 83% double bond. $C_{12}H_{23}O_5P$. Calculated %: P 11.15.

(IV) B. p. 222-224° (10 mm), $n^{20}D$ 1.4551, $d^{20}_4$ 1.1240, $MR_D$ 100.2; calculated 99.47.

Found %: P 14.69. $C_{16}H_{34}O_8P_2$. Calculated %: P 14.90.

The saponification of (III) and (IV) was carried out in dilute hydrochloric acid in sealed tubes at 130°. In both instances the acids obtained were thick, viscous, straw-colored liquids which did not crystallize on long standing.

Ozonization. Ozonized oxygen was passed for 40 hours through a solution of 5 g of (III) in 20 ml of carbon tetrachloride, the mixture being cooled with snow. The carbon tetrachloride was drawn off under vacuum and water was added to the residue which was then heated gently on a water bath. The volatile decomposition products were gradually transferred to an aqueous-alcoholic solution of dimedone. A small amount of the dimedone derivative of acetaldehyde with an m. p. of 141° (mixed melt 141°) was obtained; the main product was the dimedone derivative of ethyl glyoxylate with an m. p. of 124°.

2. The addition of dimethyl phosphorous acid. 6 g of acid and 8.5 g of ethyl sorbate were used for the reaction. In the presence of sodium methylate the reaction took place with intense liberation of heat from the reaction mixture. A large amount of tar was formed. As a result of two distillations 3.5 g of the ethyl ester of dimethylphosphone pentene carboxylic acid was obtained.

B. p. 170-171° (20 mm), $n^{20}D$ 1.4585, $d^{20}_4$ 1.1311, $MR_D$ 60.33; calculated 60.42.

Found %: P 12.70, 12.35. 85% double bond. $C_{10}H_{19}O_5P$. Calculated %: P 12.40.

### The Addition of Dialkyl Phosphorous Acids to 3,5-Heptadiene-2-One

1. The addition of diethyl phosphorous acid. The reaction was carried out with 9 g of ketone and 11.5 g of diethyl phosphorous acid in the presence of sodium ethylate. The temperature of the reaction mixture rose to 92°. The alcoholate was added for as long as its addition resulted in the liberation of heat from the reaction mixture. As a result of two distillations 10 g of 6-(diethylphosphone)-3-heptene-2-one (V) was obtained.

B. p. 163-164° (14 mm), $n^{20}D$ 1.4549, $d^{20}_4$ 1.0542, $MR_D$ 63.72; calculated 63.40.

Found %: P 12.72, 12.90. 84% double bond. $C_{11}H_{21}O_4P$. Calculated %: P 12.50.

Ozonization. 5 g of the product was ozonized in 20 ml of carbon tetrachloride for 50 hours. The ozonide was decomposed by heating with water. Methyl glyoxal was found in the decomposition products; the dimedone derivative of this substance has an m. p. of 165°. A mixed melt with the dimedone derivative of methyl glyoxal (obtained by ozonization of mesityl oxide) showed no depression of the melting point.

The addition of dimethyl phosphorous acid. 13.5 g of dimethyl phosphorous acid and 13.5 g of ketone were used for the reaction. 7 g of 6-(dimethylphosphone)-3-heptene-2-one and a considerable amount of tar were obtained.

B. p. 153-155° (11 mm), $n^{20}D$ 1.4635, $d^{20}_4$ 1.1184, $MR_D$ 54.23; calculated 54.17.

Found %: P 13.86, 13.92. 93% double bond. $C_9H_{17}O_4P$. Calculated %: P 14.09.

As a result of the saponification of 6-(dimethylphosphone)-3-heptene-2-one with dilute hydrochloric acid phosphoneheptenone was obtained in the form of a viscous liquid which did not crystallize on standing.

The addition of diethyl phosphorous acid to the diethyl ester of butadiene-1,3-phosphinic acid. The reaction was carried out with 10.5 g of the ester of butadiene-1,3-phosphinic acid and 7.5 g of diethyl phosphorous acid in the presence of sodium ethylate. The reaction proceeded very vigorously. 8.6 g of di-(diethylphosphone)-butene was obtained.

B. p. 215-216° (10 mm), $n^{20}D$ 1.4559, $d^{20}_4$ 1.1280, $MR_D$ 78.91; calculated 78.88.

Found %: P 18.78. 83% double bond. $C_{12}H_{26}O_6P_2$. Calculated %: P 18.90.

## SUMMARY

The addition of dimethyl phosphorous and diethyl phosphorous acids to diene systems, activated by an electronegative group, was investigated: these systems were represented by the ethyl esters of β-vinylacrylic, sorbic and butadiene phosphinic acids and 3,5-heptadiene-2-one.

## LITERATURE CITED

[1] A. N. Pudovik, Chem. Prog. 23, 547 (1954).

[2] A. N. Pudovik and A. Kh. Iarmukhametova, Bul. Acad. Sci. USSR, Div. Tech. Sci. 1952, 902, 926, 932.

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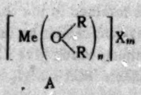
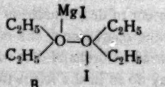
# AN INVESTIGATION OF THE THERMAL DECOMPOSITION OF ETHERATES OF MAGNESIUM IODIDE

## I. ON THE CHEMISM OF OXONIUM COMPOUNDS

V. I. Esafov

The chemical nature of etherates of metal haloid salts is examined either from the aspect of A. Werner's theory of oxonium salts [1] (formula A), adhered to by B. N. Menshutkin [2] who called these etherates "molecular compounds," or from the aspect of A. Bayer's theory of oxonium compounds. The second of these aspects was supported by N. D. Zelinskii [3] who suggested one of three possible structures (B-D) for the dietherate of magnesium iodide which he obtained, giving preference to formula (D).


A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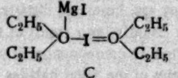
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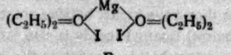
D

Later, N. S. Tsonev [4], who prepared various dietherates of $SnCl_4$ subjected several of these to thermal decomposition assuming that this would provide knowledge of their chemical structure; the investigation was, however, not completed. The method of the thermal decomposition of etherates of the haloid salts of different metals was subsequently used by many chemists [5], principally for carrying out syntheses.

The present investigation was undertaken with the object of determining the strength of the bonds of the ether molecules in the indicated compounds; the thermal decomposition method which must be given preference over other purely chemical methods was also used for this investigation.

We established that with magnesium iodide aliphatic and aliphatic aromatic ethers give dietherates (type 1) which decompose on heating to give magnesium iodide and the corresponding ether. In this connection, ethers differ widely from each other even within the limits of a homologous series. Whereas $(C_2H_5)_2O$* gives the same magnesium iodide dietherate irrespective of whether it is obtained from magnesium iodide itself or a mixture of magnesium and iodine, $(C_4H_9)_2O$, iso-$(C_5H_{11})_2O$, and also $C_6H_5OC_2H_5$ give, in addition to dietherates of the 1st type, dietherates of the 2nd type which are obtained by the action of ethers on a mixture of magnesium and iodine or by an exchange reaction.

$$2\ ROR + MgI_2 \cdot 2(C_2H_5)_2O \longrightarrow MgI_2 \cdot 2ROR + 2(C_2H_5)_2O$$

As a result of the thermal decomposition of dietherates of the 2nd type only half the ether is recovered and the other half undergoes fundamental changes. At the same time half the iodine used for the formation of magnesium iodide remains combined with the magnesium. Oxygen compounds of magnesium are found in the dry residues from the decomposition of dietherates of this type; this is proven by the fact that ammonia is literated when the dry residues are triturated with moist ammonium chloride.[*] On the basis of experimental data dietherates of the 2nd type must be considered as oxonium salts with structure (I) or (II).

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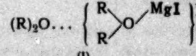
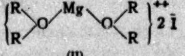
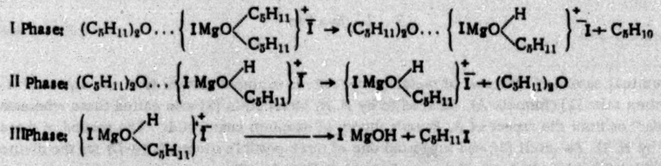
* Evidently $(CH_3)_2O$ and $C_2H_5OCH_3$ also.


(I)


(II)

The problem as to whether they are formed simultaneously in known proportions or whether only one salt, say (II),[**] is first formed, undergoing rearrangement on heating to salt (I), remains open. When $MgI_2 \cdot 2(C_4H_9)_2O$ decomposes unstable 2,3-diiodobutane is formed; this is best explained on the basis of formula (II). The general course of the decomposition of this dietherate and of $MgI_2 \cdot 2$ iso-$(C_5H_{11})_2O$, in particular, is, however, in closest agreement with the system in which the initial substance is given structure (I).



It is possible that the second molecule of ether which is less firmly combined or becomes so on heating, splits off at the very commencement of decomposition and is retained in the reaction mass, being a substance with a rather high boiling point; the character of the entire system cannot be essentially modified, however, as a result of this. It could be assumed beforehand that when ethers, which give dietherates of the 2nd type with magnesium and iodine, react they do so in the following manner: $ROR + MgI_2 \rightarrow RI + ROMgI$.

In this case the alkyl iodides would be distilled first; they are, however, distilled at the end of the decomposition after the ethers since they have higher boiling points. Finally, as a result of the decomposition of iso-$C_5H_{11}OMgI \cdot 2(C_2H_5)_2O$ (see below) isoamyl iodide is also formed; in consequence, if an ether gave rise to a mixture of alkyl halide with magnesium halide alcoholate the yields of the alkyl halides must, if not exceed then at least approximate 100% on calculating the conversion of one radical of ether to alkyl halide. Facts do not confirm this hypothesis, however. On the basis of all that has been said above we consider that the proposed system of the conversions of dietherates of magnesium iodide of the 2nd type is confirmed by all the experimental data obtained.

## EXPERIMENTAL[***]

The etherates of $MgI_2$ were prepared in a tubular Würtz flask from 2.4 g of carefully dried magnesium and 25.3 g of sublimed iodine or from 0.1 mole of $MgI_2$ and absolutely dry ethers in amounts calculated for obtaining $MgI_2 \cdot 2ROR$. The reaction of magnesium with iodine in the presence of ethers proceeds exothermically at first and requires external cooling; toward the end, however, it is necessary to heat the reaction mass to 60-70° in order to completely dissolve the magnesium. The apparatus for the decomposition of the $MgI_2$ etherates consisted of the above-mentioned flask in the neck of which a dropping funnel, plugged by a calcium chloride tube, was inserted. The tube served for installing the thermometer, the bulb of which was immersed in the reaction mass. The flask was connected to a condenser at the end of which was an adapter with an outlet pipe. A measuring cylinder was connected to the adapter by a cork; this served to collect the liquid products which passed into the cooling mixture of snow and ice during the experiments. 2 U-tubes containing calcium chloride, a Tishchenko bottle, a wash bottle and another Tishchenko bottle were connected to the outlet pipe of the adapter.

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[*] For purposes of brevity this information is not given for the individual experiments in the experimental section.

[**] In which, in spite of the symmetrical structure, the bonds of the magnesium with the oxygen may not be of equal strength.

[***] With the cooperation of the students G. F. Pologov and D. S. Shliapnikov.

The entire system was connected to a gas meter filled with a saturated solution of common salt. The flask was heated on a bath containing Wood's alloy.

I. Experiments on the decomposition of $MgI_2 \cdot 2(C_2H_5)_2O$.[*] a) To obtain 0.1 mole of $MgI_2 \cdot 2(C_2H_5)_2O$ the above-mentioned amounts of magnesium and iodine were used but in order to accelerate the dissolution of the magnesium 50% more than the standard amount of ethyl ether, i.e., 30 ml, was added. After the excess ether had been removed and the mixture cooled the dietherate crystallized immediately. After the dietherate had been carefully dried in a vacuum desiccator the m. p. was 48-50°.

Found %: I 59.09. $MgI_2 \cdot 2(C_2H_5)_2O$. Calculated %: I 59.30.

0.1 mole of the diethylate of magnesium iodide was decomposed. Its complete decomposition took place at 160-165° (temperature of the bath). As a result a total of 19-20 ml of a liquid slightly colored by iodine was obtained and a dry, white residue was left in the flask. To remove the iodine the liquid extract was shaken with mercury after which it distilled completely at 35°. The liquid had $d^{20}_4$ 0.7138 and dissolved in concentrated hydrochloric acid without leaving a residue. The liquid distillate therefore consisted of one ether and, in consequence, the dietherate of magnesium iodide decomposed into its components. The crystalline dietherate with an m. p. of 48-50° was again readily obtained by adding 20 ml of absolute ether to the dry residue in the flask. The dietherate prepared on this occasion from ready-made $MgI_2$ decomposed at the above-mentioned temperature into magnesium iodide and ether.

b) The decomposition of $MgI_2 \cdot 2(C_2H_5)_2O$, treated with water.[**] When 3.6 g of water was added carefully to 0.1 mole of $MgI_2 \cdot 2(C_2H_5)_2O$ heat was evolved, the crystals disappeared and an amorphous mass was formed. The product obtained was heated to 100°, an average of 10 ml of liquid distilling over during this process; 6.5 g of ethyl ether and 2.0 g of a liquid with a b. p. of 55-73° were isolated from this liquid by fractionation. By subsequent heating to 150° a further 9 g of liquid was distilled, from which 1.2 g of ethyl ether and 12 g of a liquid with a b. p. of 55-74° were obtained. Finally, in the third stage of decomposition from 150-220° 5 ml of liquid intensely colored by iodine, was obtained. The dry residue in the flask weighed 10.5 g. The progress of the decomposition of the dietherate of magnesium iodide, treated with water, indicates that the latter first drives out one molecule of ether from it but that the second molecule of ether undergoes chemical conversion. All the liquid products with a b. p. above 55° were combined together, treated with a solution of hyposulfite, water, concentrated hydrochloric acid (to remove ether), a solution of alkali and water and dried with $CaCl_2$. On the average (of three experiments) 16.5 g of a colorless liquid with a b. p. of 71-72°, $d^{20}_4$ 1.9306 was obtained.

Found %: I 80.81. $C_2H_5I$. Calculated %: I 81.38.

The yield of ethyl iodide was 52.6%, calculated on the assumption of the complete conversion of both ethyl radicals of the ether molecule into ethyl iodide. A weighed sample of the dry residue[***] was treated with boiling water and after it had cooled was carefully acidified with dilute $HNO_3$. The solution was filtered from the carbonaceous residue which was repeatedly washed with water. The filtrate and the wash water were made up to 250 ml; to determine the iodine ion content 10 ml of the solution was, therefore, taken on each occasion. The titration was carried out with a 0.1 N solution of $AgNO_3$ in the presence of eosin. 62.86% I was found.

II. The reaction of dibutyl, diisoamyl and phenylethyl ethers with $MgI_2$. 0.2 mole of the above-mentioned ethers was added to 0.1 mole of $MgI_2$ and to complete the reaction heating was carried out for a long period at 120-130° for the first two ethers and at 140-150° in the case of phenetole. The crystalline substances obtained were subjected to decomposition up to a maximum temperature of 265°. The initial ethers were obtained unchanged in the distillates. Consequently, ethers with ready made $MgI_2$ yield dietherates which decompose into magnesium iodide and ether.

III. The reaction of dibutyl and diisoamyl ethers with $MgI_2 \cdot 2(C_2H_5)_2O$. In each individual experiment 0.1 mole of the ether with the heavier radicals was added to 0.1 mole of $MgI_2 \cdot 2(C_2H_5)_2O$ and heating was carried out for 2.5 hours at 130° (bath) for the first and 150° (bath) for the second ether. During this process the liquid distilled over, 6.5 g being collected on the average. It distilled at 35° and dissolved completely in concentrated hydrochloric acid. A further 0.1 mole of the appropriate ether was then added and heating was continued at the same temperature until the distillation of the liquid had quite finished; an average of 5.6 g of the latter was collected. This was again ethyl ether with a b. p. of 35° which had been driven out of the compound. Ethers with heavier radicals of a primary character therefore displace ethyl ether from $MgI_2 \cdot 2(C_2H_5)_2O$ molecule by molecule. The $MgI_2 \cdot 2(C_4H_9)_2O$ and $MgI_2 \cdot 2iso\text{-}(C_5H_{11})_2O$ obtained by the exchange reaction were then subjected to decomposition. In view of the fact that the decomposition of similar dietherates leads to exactly the same products obtained from dietherates prepared by the action of dibutyl or diosoamyl ethers on a mixture of magnesium and iodine we give data characterizing the process of decomposition of dietherates obtained by the latter method.

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[*] With the cooperation of I. D. Frolov.

[**] With the cooperation of P. N. Gorelov.

[***] The analyses of the dry residues in the other experiments were carried out in exactly the same manner.

IV. Thermal decomposition of $MgI_2 \cdot 2(C_4H_9)_2O$. Dibutyl ether with the following characteristics was used:

B. p. 139.5-139.9° (739 mm), $d^{20}_4$ 0.7705, $n^{20}D$ 1.3991, $MR_D$ 40.86; calculated 40.67.

Complete solution of the magnesium was obtained by reacting 2.4 g of magnesium and 25.3 g of iodine with 26 g of dibutyl ether. The dietherate obtained in the form of a very viscous dark-colored mass was heated. At 102-105° (in the flask) decomposition commenced with evolution of gas, 370 ml of the latter being collected (16°, 739 mm). Decomposition was completed at 270°. 33.5 g of a liquid distillate, intensely colored by iodine, and 18.1 g of dry residue were obtained. In view of the fact that the gas was decolorized by bromine water it (collected from three experiments) was passed through bromine. The crude dibromide was washed with a solution of alkali, then with water and was dried with $CaCl_2$. After it had been filtered the dibromide was distilled; it passed over completely at 158-160°, corresponding to the properties of 2,3-dibromobutane. The butyl radical forming during the course of decomposition was, therefore, stabilized in the form of butene-2. To remove iodine the liquid distillate was washed with a solution of hyposulfite and water and dried with $CaCl_2$. After 2 days, however, the product became dark again as a result of the liberation of iodine. After a second purification the colorless product evolved iodine and gas (which was found to be butene-2) during distillation.

From these data it is evident that the decomposition of the dietherate was accompanied by the formation of 2,3-diiodobutane from the butene-2 and iodine. To remove this diiodobutane the liquid product was heated until the liberation of butene-2 ceased. The liquid product was then shaken with mercury and was finally distilled in a fractionating column. The following main fractions were obtained: 1st, b. p. 129-131°, $d^{20}_4$ 1.6040, 14 g; 2nd, b. p. 139-140°, $d^{20}_4$ 0.8010, 15 g. The yield of butyl iodide was 76% (calculated assuming the conversion of one butyl radical into butyl iodide). The dry residue contained 75.92% (13.7 g) of iodine and 2.16% carbonaceous residue. This proves that of the two atoms of iodine in the magnesium iodide only one took part in the chemical conversions.

V. The thermal decomposition of $MgI_2 \cdot 2iso\text{-}(C_5H_{11})_2O$. Diisoamyl ether with the following characteristics was used:

B. p. 169.5-170.5° (731 mm), $d^{20}_4$ 0.7803, $n^{20}D$ 1.4090, $MR_D$ 50.11; calculated 49.90.

0.1 mole of $MgI_2 \cdot 2iso\text{-}(C_5H_{11})_2O$, prepared from 2.4 g of magnesium 25.3 g of iodine and 31.7 g of diisoamyl ether was subjected to decomposition. At 135° (in the flask) a readily-boiling liquid began to distill over (first phase of decomposition).* In the 173-185° temperature range (second phase of decomposition)* diisoamyl ether distilled over and, finally, in the 185-260° range (third phase of decomposition)* a heavy liquid (isoamyl iodide) distilled. 42.0 g of liquid distillate was obtained and 16.0 g of dry residue was left in the flask. The following fractions were obtained from the liquid product: 1st fraction, b. p. 28-38°, 3.7 g; 2nd fraction, b. p. 146-148°, 17 g; 3rd fraction, b. p. 168-170°, 16.5 g. After it had been distilled over sodium the product with a b. p. of 28-38° had $d^{20}_4$ of 0.6570 and an iodine number, according to Hanus, of 274.5. The given fraction therefore consisted of about 75% isoamylene. The high boiling point of the fraction indicated the presence in it of trimethylethylene. To investigate this problem Fraebe and Hochsteller's method [6] was tried. A dibromide which was subsequently boiled with water was obtained from 3 g of the substance with a b. p. of 28-38°. Finally, 1.2 g of a product with a b. p. of 90-94° was obtained; the semicarbazone made from this had an m. p. of 112°. The constants of the substance and the semicarbazone correspond to methyl isopropyl ketone. This proves that the fraction with a b. p. of 28-38° contains trimethylethylene, the dibromide of which is converted to methyl isopropyl ketone when boiled with water. In consequence, at the moment of splitting off the isoamyl radical, losing an atom of hydrogen, is stabilized mainly in the form of trimethylethylene. The fraction with a b. p. of 146-148° had $d^{20}_4$ of 1.4275.

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* From the data of special experiments in which the liquid products of the individual phases were obtained.

Found %: I 64.47. $C_5H_{11}I$. Calculated %: 64.70.

The yield of isamyl iodide was 85.9%. The fraction with a b. p. of 168-170° had $d^{20}_4$ of 0.7813 and was the initial diisoamyl ether. The amount of recovered ether indicates that of the two molecules of diisoamyl ether included in the dietherate only one took part in chemical conversions. The dry residue was analyzed; it contained 70.67% (10.74 g) of iodine and 5.08% of a carbonaceous residue.

VI. The thermal decomposition of $MgI_2 \cdot 2C_6H_5OC_2H_5$. Phenetole with the following characteristics was used:

B. p. 165° (722mm), $d^{20}_4$ 0.9622, $n^{20}D$ 1.5077, $MR_D$ 37.33; calculated 37.06.

The dietherate obtained by the reaction of 2.4 g of magnesium, 25.3 g of iodine and 24.5 g of phenetole was subjected to decomposition up to a temperature of 260°; 34.3 g of liquid distillate, containing 6.6 g of free iodine. After the treatment of the distillate with a solution of hyposulfite and water, followed by drying with $CaCl_2$, it was fractionated. Finally, 10.9 g of ethyl iodide with a b. p. of 72-73°, $d^{20}_4$ 1.9083 and 10.5 g of phenetole with a b. p. of 164-166° were obtained. 3 g of crystalline phenol with an m. p. of 40° was extracted from the condenser. The residue in the flask was a dark tarry mass weighing 17.5 g. It contained 41.7% iodine. Taking into account the free iodine liberated and the iodine in the dry residue it is evident that in this instance only half the iodine used for the reaction takes part in the conversions. Likewise, out of two ether molecules one is recovered unchanged.

VII. The thermal decomposition of iso-$C_5H_{11}OMgI \cdot 2(C_2H_5)_2O$. The Grignard reagent prepared from 2.4 g of magnesium and 18 g of $CH_3I$ in 40 ml of absolute ether was heated in a bath at 100° to remove excess ether and methyl iodide. After it had cooled, 8.5 g of anhydrous isoamyl alcohol was carefully added. As a result of this operation 2345 ml* of methane (17°, 732 mm) was obtained. The flask with the etherate was then heated up to 235°; 25.5 ml of liquid extract was obtained; the dry residue in the flask weighed 14.4 g and contained 66.85% iodine. $^2/_3$ of the iodine used for the reaction therefore remained chemically combined with the magnesium. To remove the ethyl ether the liquid distillate was treated with concentrated hydrochloric acid, then with a weak solution of alkali and water and dried with $CaCl_2$. After it had been fractionated the following fractions were obtained: 1st fraction, 32-35°, 2.4 g, $d^{20}_4$ 0.6580 (this fraction reacted vigorously with bromine); 2nd, 70-73°, 1.5 g, $d^{20}_4$ 1.8900; 3rd, 73-146°, 3.2 g; 4th, 146-148°, 2.3 g, $d^{20}_4$ 1.4170. During the course of the decomposition of iso-$C_5H_{11}OMgI \cdot (C_2H_5)_2O$ isoamylene, ethyl iodide and isoamyl iodide were, therefore, obtained. In view of the small amount present the nature of the products included in the intermediate fraction with a b. p. of 73-146° was not investigated in greater detail.

## SUMMARY

1. It was established that with $MgI_2$, ethers give dietherates with a weak bond between the magnesium and the oxygen of the ether molecules, as a result of which they are decomposed on heating into $MgI_2$ and ether.

2. It was shown that ethers differ among themselves with regard to their capacity to form dietherates of $MgI_2$ with different properties. Some ethers form the same dietherate of $MgI_2$ irrespective of whether the latter is made from $MgI_2$ or a mixture of magnesium and iodine. The second group of ethers gives two types of dietherates of $MgI_2$: the first of these is obtained from $MgI_2$, the second from a mixture of magnesium and iodine or by driving out ethyl ether from $MgI_2 \cdot 2(C_2H_5)_2O$.

3. It was shown that ethers with heavier primary radicals displace ethers with lighter radicals from $MgI_2 \cdot 2R_2O$.

4. It was shown that the thermal decomposition of dietherates of $MgI_2$ of the 2nd type with aliphatic ethers is accompanied by the formation of olefins and alkyl iodides, one molecule of ether and one atom of iodine taking part in the chemical conversions. The second atom of iodine remains firmly combined with the magnesium.

5. It was shown that in the thermal decomposition of dietherates of $MgI_2$ of the 2nd type with aliphatic-aromatic ethers alkyl halides, phenols and a tarry mass are formed. One molecule of the aliphatic-aromatic ether is liberated in the free state.

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* As in original — Publisher's note.

6. The presence of a stable chemical bond between the magnesium and the oxygen of one molecule of ether in dietherates of $MgI_2$ of the 2nd type indicates their oxonium nature.

7. A system for the thermal decomposition of dietherates of the 2nd type was given.

## LITERATURE CITED

[1] A. Werner, New Opinions in the Field of Inorganic Chemistry, Leningrad, ONTI,230 (1936).*

[2] B. N. Menshutkin, J. Russ. Chem. Soc. 35, 610 (1903); J. Russ. Chem. Soc. 37, 1090, 1186 (1905); J. Russ. Chem. Soc. 38, 554, 1229, 1317, 1335 (1906).

[3] N. D. Zelinskii, J. Russ. Chem. Soc. 35, 399 (1903).

[4] N. S. Tsonev, J. Russ. Chem. Soc. 48, 550 (1916).

[5] G. L. Stadnikov and L. I. Kashtanov, J. Russ. Chem. Soc. 60, 1177 (1928); L. I. Kashtanov, J. Gen. Chem. 2, 515 (1932); I. Kozlov, R. Bogdanovskaia and N. Sologub, J. Gen. Chem. 6, 315 (1936); R. R. Galle, J. Gen. Chem. 8, 402 (1938); Ia. L. Gol'dfarb and I. Smorgonskii, J. Gen. Chem. 8, 1516 (1938); M. Dangian, J. Gen. Chem. 10, 1885 (1940), 11, 1215 (1941).

[6] Fraebe u. Hochsteller, Monatsh. 23, 1075 (1902).

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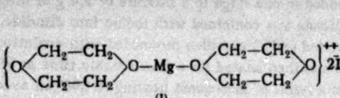
* Russian translation.

# AN INVESTIGATION OF THE THERMAL DECOMPOSITION OF THE REACTION PRODUCTS OF DIOXAN WITH MAGNESIUM IODIDE DIETHERATE, MAGNESIUM IODIDE AND A MIXTURE OF MAGNESIUM AND IODINE

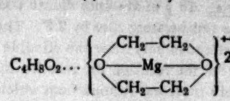
## II. ON THE CHEMISM OF OXONIUM COMPOUNDS

V. I. Esafov

The fact having been established that with magnesium iodide, ethers give compounds of the type $MgI_2 \cdot 2ROR$, which decompose on heating into the initial components,* it was worth investigating similar compounds containing dioxan. It was first established that the action of dioxan on $MgI_2 \cdot 2(C_2H_5)_2O$ and $RMgHal \cdot 2(C_2H_5)_2O$ [2] is completely analogous, i.e., the dioxan displaces equimolecular ethyl ether from them. In contrast to ethers the compound which dioxan forms with $MgI_2$, $MgI_2 \cdot 2C_4H_8O_2$, only liberates half its dioxan on heating and the other half undergoes decomposition. The oxygen atoms of dioxan therefore have a greater capacity for the formation of oxonium salts than the oxygen atoms of ethers and, in consequence, give more stable oxonium compounds. Dioxan gives the most typical oxonium compound when it acts on a mixture of magnesium and iodine. This substance must be considered as a dioxonium salt with a symmetrical (I) or an unsymmetrical (II) structure



(I)



(II)

The problem as to whether these salts are formed simultaneously or whether only the (I) salt is initially formed and is then converted to salt (II) on heating remains unsolved. One thing is clear, namely that if salt (I) kept its structure on heating, β,β'-diiododiethyl ether would be found in the decomposition products; this was not found during the experiments. On the contrary, the experimental data are in complete agreement with structure (II). Among the decomposition products of this salt were found dioxan, ethylene, ethylene iodide, ethyl iodide, acetaldehyde, iodine and magnesium oxide. Finally, data on the reaction of dioxan with a mixture of magnesium and iodine prove that like ethers dioxan did not react in this instance according to the system

$$C_4H_8O_2 + MgI_2 \rightarrow C_2H_4I_2 + C_2H_4O_2Mg,$$

because instead of the readily-melting ethylene iodide the infusible dioxonium salt was actually obtained.

### EXPERIMENTAL**

1. The thermal decomposition of $MgI_2 \cdot 2C_4H_8O_2$, obtained by the action of dioxan on $MgI_2 \cdot 2(C_2H_5)_2O$. The experiments were carried out in the apparatus described previously [1]. 9 g of absolute dioxan was added with stirring to 0.1 mole of $MgI_2 \cdot 2(C_2H_5)_2O$, heated to 50° and the substance obtained was heated at 115-120°

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* See paper I [1].

** With the cooperation of the student V. D. Kharochkin.

until the distillation of the liquid ceased. In this process an average of 9 ml (6.5 g) of liquid distillate was obtained; this distilled almost completely at 35° and dissolved completely in concentrated hydrochloric acid. A further 9 g of dioxan was added to the product, cooled to 50° and the mixture was heated to 125-130° until the distillation of liquid ceased, 10.5 ml (7.8 g) of the latter being obtained on the average; with the exception of a few drops this liquid consisted of ethyl ether. The $MgI_2 \cdot 2C_4H_8O_2$, obtained by driving out ethyl ether, was a white solid product of greatly increased volume which was subjected to decomposition up to a limit of 355°. 1.76 liters of gas (17°, 743 mm), containing 76.3 vol. % ethylene, 12.4 g of a dark-colored liquid distillate, 2.5 g of a crystalline product mixed with iodine and 26.4 g of a dry residue were obtained. The following fractions were obtained from the liquid distillate: 1st, up to 40°, 1.5 g; 2nd, 70-72°, 1.1 g, $d^{20}_4$ 1.8992; 3rd, 99-100°, 7.2 g; the residue was 2.2 g. The 1st fraction gave a positive reaction with fuchsine sulfurous acid, the 2nd fraction consisted of ethyl iodide, the 3rd fraction which did not enter into the reaction with dioxan had a $d^{20}_4$ of 1.0340. The crystalline substance and the residue from the distillates of the liquid products were treated with a solution of KI until the iodine was completely removed. The solution of iodine in KI obtained required 280.0 ml of a 0.1 N solution of $Na_2S_2O_3$, corresponding to 3.554 g of iodine. After treatment with a solution of KI the crystalline product weighed 0.6 g (see below, Experiment 3). 7.03% carbonaceous residue, 0.72 g of free and 18.76 g of combined iodine were found in the analysis of the dry residue (26.4 g). When the dry residue was triturated with moist ammonium chloride in a mortar ammonia was liberated.

2. The thermal decomposition of $MgI_2 \cdot 2C_4H_8O_2$ obtained by the action of dioxan on $MgI_2$. 18 g of absolute dioxan was added at 27° to 0.1 mole of $MgI_2$; the temperature rose by 1°. To complete the reaction the mixture was heated for 6 hours at 80°. Finally, a white solid mass was obtained which was subjected to decomposition up to a limit of 325°. Distillation of the liquid commenced at 94°, the liberation of gas began at 244°. After decomposition 1.2 liters (19°, 743 mm) of gas was obtained; this contained 60.3 vol. % ethylene, 14.8 g of a dark liquid distillate, 1.2 g of a crystalline product (see below, Experiment 3) and 27.0 g of dry residue. As a result of fractionation the following fractions were obtained from the liquid distillate: 1st, up to 40°, 0.3 g, giving a positive reaction with fuchsine sulfurous acid;* 2nd, 70-72°, 0.4 g; 3rd, 99-100°, 10.7 g; 2.1 g of a residue consisting almost entirely of iodine. 5.2% of carbonaceous residue, 2.9 g of free and 20.0 g of combined iodine were found in the dry residue.

3. The thermal decomposition of $MgI_2 \cdot 2C_4H_8O_2$ obtained by the action of dioxan on a mixture of magnesium and iodine. 18 g of absolute dioxan was added in one stage to a mixture of 2.4 g of magnesium and 25.3 g of iodine. The temperature rose by 2.5°. The dioxan was combined with iodine into diiodide, the reaction with magnesium commenced only after the diiodide melted (~85°) and then proceeded with evolution of heat up to 112°. To complete the reaction the reaction mass was then heated for a considerable time at 95-100°. Finally, a spongy, infusible mass was formed from which, as a result of subsequent heating to 200°, an average of 9.5 g of dioxan with a b. p. of 99-100° (737 mm), $d^{20}_4$ 1.0300** was obtained. This fact proves that of the two molecules of dioxan only one is subjected to fundamental chemical conversions. Decomposition was completed at 365°, the temperature being kept within the 355-365° range for 1.5 hours towards the end of the reaction. 1.6 liters of gas (19°, 732 mm), containing 70.2 vol. % ethylene, was obtained. A dibromide was obtained from the gas collected from all the experiments:

B. p. 130-131°, $d^{20}_4$ 2.1757, $n^{20}D$ 1.5315, $MR_D$ 26.51; calculated 26.96.

The liquid distillate contained iodine and a crystalline substance which was filtered through a glass filter. After it had been fractionated the filtrate gave the following fractions: 1st, up to 40°, 0.3 g; 2nd, 70-72°, 1.7 g, $d^{20}_4$ 1.9008; 3rd, 99-100°, 8.4 g, $d^{20}_4$ 1.028, and a residue. The condenser and the adapter of the decomposition apparatus were filled with a crystalline substance mixed with iodine. This mixture, the crystalline substance from the filter and the residue from the fractionations were treated with a solution of KI to remove iodine. The solution obtained contained 9.95 g of free iodine. The crystalline substance was dried in a vacuum desiccator and weighed 8 g. After it had been crystallized from petroleum ether it was obtained in the form of long (>1 cm) colorless needles with an m. p. of 81°; these were analyzed.

Found %: I 89.76. $C_2H_4I_2$. Calculated %: I 90.05.

The yield of ethylene iodide was 28.3%. The dry residue from the decomposition (14.7 g) contained 6.5 g of combined iodine. When it was triturated with moist ammonium chloride ammonia was liberated. The first fractions with a boiling point of up to 40° were mixed with the water from the wash bottles and treated with a solution of $KMnO_4$. The filtrate from the $MnO_2$ was made alkaline and was evaporated to dryness. The potassium salts were decomposed with dilute sulfuric acid after which the organic acids were steam distilled. The aqueous solution of the latter was saturated with $Ag_2CO_3$. The solution of the Ag salts was condensed until crystallization commenced. The Ag salt, dried at 85° to constant weight, contained 64.4% Ag. The data obtained prove the presence of acetaldehyde in the water of the wash bottles and the fraction up to 40°.

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* The water in the wash bottles also gave a positive aldehyde reaction.

** Data of a special experiment.

## SUMMARY

1. It was shown that dioxan displaces ethyl ether equimolecularly from $MgI_2 \cdot 2(C_2H_5)_2O$.

2. In contrast to aliphatic and aliphatic-aromatic ethers with $MgI_2$ dioxan gives an oxonium compound with a more stable bond of the magnesium with the oxygen.

3. It was shown that as a result of the decomposition of $MgI_2 \cdot 2C_4H_8O_2$ half the dioxan is reliberated while the other half forms ethylene, ethylene iodide, ethyl iodide and acetaldehyde.

## LITERATURE CITED

[1] V. L. Esafov, J. Gen. Chem. 28, 1212 (1958).*

[2] W. Schlenk, W. Schlenk, Jr., Ber. 62, 920 (1929).

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* Original Russian pagination. See C. B. Translation.

# THE SYNTHESIS AND INVESTIGATION OF THE CHLORINATION PRODUCTS OF ACETYLENYLDIVINYL (1,3-HEXADIENE-5-INE)

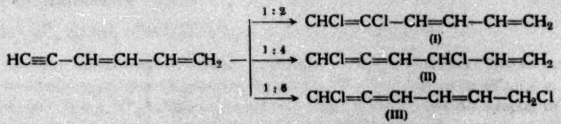
A. N. Akopian, A. M. Saakian and M. G. Avetian

It is known [1] that when vinylacetylene is obtained by the low-temperature polymerization of acetylene a certain amount of divinylacetylene is formed, the actual quantity depending on the conditions of the process. As was shown by A. L. Klebanskii and his co-workers [2], the divinylacetylene obtained contains 15-20% of its isomer, acetylenyldivinyl. The latter was subjected to hydrochlorination [2], hydration [3] and hydrogenation [4]. It was shown that it readily polymerizes and reacts with oxygen twice as rapidly as divinylacetylene, forming explosive peroxides. There are no data in literature on the chlorination of acetylenyldivinyl whereas the chlorination of divinylacetylene has been investigated in detail [5]. It was shown that during the process of the chlorination of divinylacetylene its di-, tetra- and hexachloro derivatives are formed and that the formation of each succeeding compound from the previous one takes place by the addition of chlorine in the 1,4 position, i.e., at the ends of the conjugate enoid compound or diene. It is possible that the cause of this phenomenon is the symmetrical structure of divinylacetylene.

Acetylenyldivinyl is distinguished from divinylacetylene by the unsymmetrical structure of the molecules; it would, therefore, be expected that it would chlorinate in a different manner. In our laboratory it was repeatedly found that divinylacetylene chlorinates far more rapidly than acetylenyldivinyl.

The investigation of the chlorination reaction of acetylenyldivinyl, apart from the preparation and description of the new compounds of this series and the elucidation of the reaction mechanisms, can also be of use if technical divinylacetylene is utilized by means of its chlorination and the subsequent processing of the chloro derivatives.

Depending on the direction of addition of the chlorine, as a result of the chlorination of acetylenyldivinyl the formation of dichloro derivatives with the following structure would be expected:



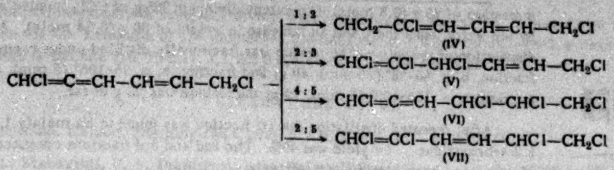
$$HC{\equiv}C{-}CH{=}CH{-}CH{=}CH_2 \xrightarrow{1:2} CHCl{=}CCl{-}CH{=}CH{-}CH{=}CH_2 \quad \text{(I)}$$

$$HC{\equiv}C{-}CH{=}CH{-}CH{=}CH_2 \xrightarrow{1:4} CHCl{=}C{=}CH{-}CHCl{-}CH{=}CH_2 \quad \text{(II)}$$

$$HC{\equiv}C{-}CH{=}CH{-}CH{=}CH_2 \xrightarrow{1:6} CHCl{=}C{=}CH{-}CH{=}CH{-}CH_2Cl \quad \text{(III)}$$

Other possible directions of the reaction, in which the triple bond remains unaffected, do not seem very probable to us. The fact that chloroacetic acid was formed as a result of the oxidation by potassium permanganate of the dichloride obtained from acetylenyldivinyl and that an atom of chlorine was split off by the action of a hot aqueous solution of sodium carbonate on the dichloro derivative indicates that the addition of the first molecule of chlorine to acetylenyldivinyl takes place in the 1,6 position, the result being the formation of 1,6-dichloro-1,2,4-hexatriene (III).

Depending on the direction of addition of the chlorine, the conversion of the dichlorohexatriene formed into the tetrachloride would lead to compounds of the following structure



$$\mathrm{CHCl{=}C{=}CH{-}CH{=}CH{-}CH_2Cl} \xrightarrow{1:2} \underset{\text{(IV)}}{\mathrm{CHCl_2{-}CCl{=}CH{-}CH{=}CH{-}CH_2Cl}}$$

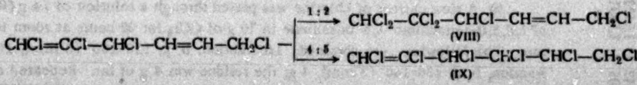
$$\xrightarrow{2:3} \underset{\text{(V)}}{\mathrm{CHCl{=}CCl{-}CHCl{-}CH{=}CH{-}CH_2Cl}}$$

$$\xrightarrow{4:5} \underset{\text{(VI)}}{\mathrm{CHCl{=}C{=}CH{-}CHCl{-}CHCl{-}CH_2Cl}}$$

$$\xrightarrow{2:5} \underset{\text{(VII)}}{\mathrm{CHCl{=}CCl{-}CH{=}CH{-}CHCl{-}CH_2Cl}}$$

The formation of chloroacetic acid as the main product in the oxidation by potassium permanganate of the tetrachlorohexadiene formed indicates that the double bond between the 4 and 5 carbon atoms remains unaffected, i.e., substances (VI) and (VII) are out of the question and the decisive factor in the choice between compounds (IV) and (V) is the fact that as a result of the action of a hot aqueous solution of sodium carbonate on the tetrachloride two chlorine atoms are split off; in the conversion of 1,6-dichloro-1,2,4-hexatriene to the tetrachloride the addition of chlorine does not take place at the ends of the conjugate diene but the double bond between the 2 and 3 carbons is saturated, as a result of which 1,2,3,6-tetrachloro-1,4-hexadiene is formed.

The next chlorination product of acetylenyldivinyl is hexachlorohexene which we obtained by the direct chlorination both of acetylenyldivinyl and its tetrachloro derivative. On the basis of the structure of the initial 1,2,3,6-tetrachloro-1,4-hexadiene two hexachlorides (VIII) and (IX) can be expected.



$$\mathrm{CHCl{=}CCl{-}CHCl{-}CH{=}CH{-}CH_2Cl} \xrightarrow{1:2} \underset{\text{(VIII)}}{\mathrm{CHCl_2{-}CCl_2{-}CHCl{-}CH{=}CH{-}CH_2Cl}}$$

$$\xrightarrow{4:5} \underset{\text{(IX)}}{\mathrm{CHCl{=}CCl{-}CHCl{-}CHCl{-}CHCl{-}CH_2Cl}}$$

Unfortunately, it is impossible to establish which of these two structures corresponds to the hexachloride obtained because like the hexachloride of divinylacetylene the compound obtained is not oxidized by potassium permanganate, is not acted on by ozone and with continued ozonization splits off hydrogen chloride; this obscures the true picture. The fact that on oxidation with potassium permanganate the dichlorohexatriene and tetrachlorohexadiene preceding the hexachloride form chloroacetic acid while the hexachloride is not oxidized by potassium permanganate and chloroacetic acid is not formed indicates that the double bond between the 4 and 5 carbons has ceased to exist. We assume, therefore, that the structure of the hexachloride corresponds to (IX) and that it is 1,2,3,4,5,6-hexachloro-1-hexene.

In contrast to divinylacetylene which does not undergo complete chlorination even under the influence of sunlight and the final chlorination product of which is 1,2,3,4,5,6-hexachloro-3-hexene, acetylenyldivinyl is completely chlorinated, i.e., it gives octachlorohexane. The preparation of the latter from the hexachloride is carried out in sunlight. From its structure the expected octachloride must be 1,1,2,2,3,4,5,6-octachlorohexane

$$\mathrm{CHCl_2{-}CCl_2{-}CHCl{-}CHCl{-}CHCl{-}CH_2Cl.}$$

In consequence, as a result of the chlorination of acetylenyldivinyl the following compounds not described in literature were obtained; 1,6-dichloro-1,2,4-hexatriene, 1,2,3,6-tetrachloro-1,4-hexadiene, 1,2,3,4,5,6-hexachloro-1-hexene and 1,1,2,2,3,4,5,6-octachlorohexane. The di- and tetrachloro derivatives are very unstable liquids with a characteristic unpleasant odor. On keeping, they split off hydrogen chloride and rapidly become turbid and tarry, the first undergoing these changes in the course of several days, the last in a matter of weeks. The hexachloride is a colorless stable oily liquid with a pleasant citrus odor. Octachlorohexane is in the form of lamellar crystals with an odor of camphor.

## EXPERIMENTAL

The acetylenyldivinyl was separated from the fraction of divinylacetylene obtained by the low-temperature polymerization of acetylene with Nieuwland's catalyst [1] by a method reported in the work [2]; b. p. 79° (680 mm), $d^{20}_4$ 0.7848, $n^{20}D$ 1.5090.

The preparation of 1,6-dichloro-1,2,4-hexatriene. Chlorine was passed through a solution of 63 g (0.8 mole) of acetylenyldivinyl in 325 g of $CCl_4$, cooled externally by ice water, until there was an increase in weight of 60 g (0.84 mole). After the distillation of the solvent the residue was fractionally distilled under vacuum. 1st fraction, b. p. 60-75° (10 mm), 40 g; 2nd fraction, b. p. 75-105° (5 mm), 30 g; 3rd fraction, b. p. 105-130° (5 mm), 20 g; the residue was 25 g of tar.

After repeated distillation the 1st fraction was found to be mainly 1,6-dichloro-1,2,4-hexatriene. The yield was 40%. The 2nd and 3rd fractions consisted mainly of tetra- and hexachlorides, respectively.

The preparation of 1,2,3,6-tetrachloro-1,4-hexadiene. Chlorination was carried out in the manner described above. 40 g of acetylenyldivinyl in 200 g of $CCl_4$ was used; the chlorine was passed until there was an increase in weight of 62 g. After the solvent had been removed and the 2nd fraction fractionally distilled the latter which had a b. p. of 70-100° (2 mm) (36 g) consisted mainly of tetrachlorohexatriene. The yield was 32%.

The preparation of 1,2,3,4,5,6-hexachloro-1-hexene. a) Chlorine was passed into a solution of 47 g of acetylenyldivinyl in 250 g of $CCl_4$ until there was an increase in weight of 130 g. The following fractions were obtained: 1st fraction, b. p. up to 105° (3 mm), 15 g; 2nd fraction, b. p. 105-120° (3 mm), 76 g; the residue was 75 g of tar. The 2nd fraction consisted mainly of hexachloride. The yield was 45%.

b) A slow current of chlorine was passed through a solution of 14 g (0.063 mole) of 1,2,3,6-tetrachloro-1,4-hexadiene in 70 g of $CCl_4$ for 20 hours at room temperature. The following were obtained: 1st fraction, b. p. 110-130° (3 mm), 15 g; 2nd fraction, b. p. 130-140° (3 mm), 4 g; the residue was 4 g of tar. Repeated distillation of the 1st fraction gave 11 g (61%) of pure hexachloride.

The preparation of 1,1,2,2,3,4,5,6-octachlorohexane. A solution of 14 g of 1,2,3,4,5,6-hexachloro-1-hexene in 200 g of $CCl_4$ was saturated, while cooled with ice water, with chlorine (7.5 g) and exposed to sunlight until decolorized. The operation was repeated again with 9.9 g of chlorine. After the solvent had been removed 7 g of crystals with an m. p. of 124-125° (from methanol) was obtained.

The physical properties of the acetylenyldivinyl chlorides we obtained and the analytical data are given in Table 1.

The structure of the acetylenyldivinyl chlorides was based on the determination of the amounts of saponifiable chlorine atoms in them and by the results of oxidation with potassium permanganate.

a) A mixture of 5 g of dichloride and 7 g of $Na_2CO_3$ in 100 ml of water was boiled for 9 hours, the mixture being stirred. Analysis of the aqueous layer showed the presence of 0.033 mole of sodium chloride, corresponding to one atom of saponifiable chlorine.

b) 30 g of dichloride in 200 ml of water was reduced at 15° with 202 g of potassium permanganate for 13 hours. After the precipitate of manganese dioxide had been separated and the solution from it acidified 8 g of chloroacetic acid was extracted; after the latter had been recrystallized from petroleum ether the m. p. was 59-60° and it showed no depression of the m. p. in a mixed melt with known chloroacetic acid.

The saponification of tetrachlorohexadiene under the same conditions showed the presence of two atoms of saponifiable chlorine. The oxidation of 30 g of tetrachloride took 120 g of potassium permanganate; 8.3 g of unpurified chloroacetic acid was obtained.

| Formulas of the substances | B. p. or m. p. | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ |  | Cl content (in %) |  |
|---|---|---|---|---|---|---|---|
|  |  |  |  | found | calculated | found | calculated |
| $CHCl{=}C{=}CH{-}CH{=}CH{-}CH_2Cl$ . . . . . | 45—46° (3 mm) | 1.1640 | 1.5309 | 39.5945 | 38.241 | 47.49 | 47.65 |
| $CHCl{=}CCl{-}CHCl{-}CH{=}CH{-}CH_2Cl$ . . . . | 88—90 (3 mm) | 1.4242 | 1.5572 | 49.7423 | 48.442 | 64.68 | 64.54 |
| $CHCl{=}CCl{-}CHCl{-}CHCl{-}CHCl{-}CH_2Cl$ . . . | 110—112 (2 mm) | 1.5605 | 1.5491 | 59.3257 | 58.643 | 72.68 | 73.19 |
| $CHCl_2{-}CCl_2{-}CHCl{-}CHCl{-}CHCl{-}CH_2Cl$ . . . | M.p. 124—125° | — | — | — | — | 78.1 | 78.46 |

## SUMMARY

The chlorination products of acetylenyldivinyl were prepared and investigated. It was shown that chlorination takes place via the formation of 1,6-dichloro-1,2,4-hexatriene, 1,2,3,6-tetrachloro-1,4-hexadiene, 1,2,3,4,5,6-hexachloro-1-hexene and, finally, 1,1,2,2,3,4,5,6-octachlorohexane is obtained.

## LITERATURE CITED

[1] Nieuwland, Calcott, Downing and Carter, J. Am. Chem. Soc. 53, 4197 (1931).

[2] A. L. Klebanskii, U. A. Dranitsyna, L. M. Dobromil'skaia, Proc. Acad. Sci. USSR 1, No. 3-4, 229 (1935).

[3] I. M. Dolgopol'skii, L. M. Dobromil'skaia and K. N. Podkapaeva, J. Gen. Chem. 17, 1695 (1947).

[4] A. L. Klebanskii, L. D. Popov, N. Ia. Tsukerman, J. Gen. Chem. 16, 2089 (1946).

[5] D. D. Coffman and W. H. Carothers, J. Am. Chem. Soc. 55, 2040 (1933).

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# THE PREPARATION AND PROPERTIES OF SOME ARYL DERIVATIVES OF THIOXANTHENOL-5-DIOXIDE WITH INDICATOR PROPERTIES

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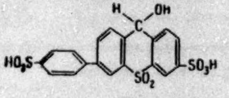
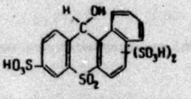
As we have previously communicated [1], under specific conditions derivatives of thioxanthenol-5-dioxide having indicator properties are obtained by the sulfonation of certain aromatic compounds of the type $Ar_2CH-R'$ where R' = H, Alk or Ar. In the development of this work it appeared to us of interest to investigate the influence of various aryl substituents on the color of the compounds obtained during sulfonation and the possibility of using them as indicators in acidimetric determinations. For this purpose we investigated the sulfonation of 4-benzyldiphenyl, α-benzylnaphthalene and α,α'-dinaphthylmethane. The sulfonation was carried out with 25-40% oleum at high temperature. As a result, sulfonic acids having indicator properties similar to those previously described [1], were obtained. In neutral and acid media solutions of these compounds remained colorless, becoming intensely colored on the addition of alkali. The change in the color of these compounds takes place at a pH of 10-11. The color of a particular compound depends on the nature of the substituent; this is evident from the absorption curves in the visible region of alkaline solutions of the above-mentioned compounds (see Fig. 1).*

The compounds obtained were easily oxidized by potassium permanganate and chromic acid, losing their capacity to change color in an alkaline medium. They can be used as indicators for titrations. The absolute error in the titration of various organic acids is on the average ± 0.3%.

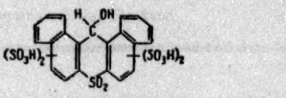
On the basis of the properties and the analysis of the compounds obtained their structure can be represented by the formulas (I-III).



(I)



(II)



(III)

## EXPERIMENTAL

Synthesis of the initial substances. 4-Benzyldiphenyl was synthesized from diphenyl and benzyl chloride in the presence of $ZnCl_2$. For this purpose 250 g of diphenyl 136 g of benzyl chloride and 70 g of $ZnCl_2$ were heated on an oil bath until the liberation of HCl ceased. The product was then extracted with ether and washed with water; after the solvent and the unreacted diphenyl had been distilled under vacuum 90 g of a hydrocarbon with a b. p. of 195-200° (4 mm) and an m. p. of 84-85° (literature data: m. p. 85° [2])was obtained.

Found %: C 93.30, 93.43; H 6.27, 6.48. $C_{19}H_{16}$. Calculated % C 93.50; H 6.50.

α-Benzylnaphthalene was obtained by a similar method [3]. α,α'-Dinaphthylmethane was synthesized from naphthalene and α,α'-dichlorodimethyl ester in nitrobenzene in the presence of $AlCl_3$, by analogy with a previously described method [4]. For this purpose 170 ml of dry nitrobenzene was introduced into a half-liter, pear-shaped, four-necked flask, equipped with a stirrer, thermometer, reflux condenser and a dropping funnel; 40 g of $AlCl_3$ was then dissolved in the nitrobenzene, cooling being employed. 89 g of pure naphthalene was then added in small portions. A mixture of 20 g of α,α'-dichlorodimethyl ester in 30 ml of nitrobenzene was then added dropwise from a dropping funnel over a period of 30 minutes, the mixture being stirred. As a result, the temperature rose from 18 to 37°. The reaction mixture was then heated on a water bath at 45-50° until the liberation of HCl had completely ceased. The contents of the flask were poured into water acidified with HCl, the nitrobenzene layer was washed with alkali and water and the nitrobenzene was steam distilled. The viscous light-yellow mass which remained was recrystallized from alcohol. 80 g (86%) of pure α,α'-dinaphthylmethane with an m. p. of 106-107° was obtained. A mixed melt with the hydrocarbon obtained by means of a Grignard reagent [5] showed no depression of the melting point.

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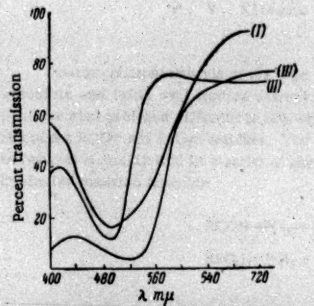
* The spectra were determined by A. M. Fisher.



Absorption curves in the visible region of the compounds (I), (II) (Ba salt) and (III) (K salt) in an aqueous solution of NaOH (pH 11.5). (Explanation in the text)

The sulfonation of 4-benzyldiphenyl. 20 g of 4-benzyldiphenyl was treated with 40% oleum, the mixture being stirred until the hydrocarbon layer disappeared. The temperature rose to 180°. The reaction mixture was poured carefully onto ice and neutralized with barium carbonate. The solution was filtered from $BaSO_4$, concentrated, filtered again and the Ba salt (I) precipitated with alcohol; the weight of the precipitate was 42 g (83%). By repeated recrystallization a perfectly pure salt was obtained.

Found %: Ba 22.17, 22.20. $C_{19}H_{12}O_9S_3Ba$. Calculated %: Ba 22.30.

The sulfonation of α-benzylnaphthalene. 25 g of α-benzylnaphthalene (m. p. 53-54°) was treated with 40% oleum until the hydrocarbon layer disappeared, the temperature rising during this process to 165°. The mixture was kept at this temperature for 15 minutes and the cooled sulfonic mass was poured onto ice. After it had been neutralized with $BaCO_3$ and filtered the solution was concentrated under vacuum and the Ba salt (II) was precipitated with alcohol. 62 g of salt was obtained, representing a yield of 70%. The ammonium salt (II) was obtained by precipitating the $Ba^{2+}$ with a saturated solution of $(NH_4)_2SO_4$.

Found %: $NH_4$ 9.20, 9.18. $C_{17}H_{21}O_{12}N_3S_4$. Calculated %: $NH_4$ 9.20.

Found %: Ba 27.52, 27.65. $(C_{17}H_9O_{12}S_4)_2Ba_3$. Calculated %: Ba 27.82.

The sulfonation of α, α'-dinaphthylmethane. 9.77 g of α,α'-dinaphthylmethane (m. p. 108-109°) was treated with 63 g of 25% oleum, the mixture being cooled. It was then heated to 120° and kept at this temperature for 20 minutes. The mass was cooled and poured onto ice. It was neutralized with $BaCO_3$, filtered, concentrated on a water bath and the Ba salt (III) was precipitated with alcohol, the weight obtained being 24 g (71.0%). The ammonium salt was also prepared and analyzed.

Found %: Ba 29.43, 29.12. $C_{21}H_{10}O_{15}S_5Ba_2$. Calculated %: Ba 29.20.

Found %: $NH_4$ 9.55, 9.60. $C_{21}H_{10}O_{15}S_5(NH_4)_4$. Calculated %: $NH_4$ 9.80.

## SUMMARY

1. A method was developed for synthesizing sulfonic acids of thioxanthenol-5-dioxide derivatives by the sulfonation of 4-benzyldiphenyl, α-benzylnaphthalene and α,α'-dinaphthylmethane with oleum at high temperature.

2. It was shown that the above-mentioned compounds can be used as indicators for acidimetric determinations.

3. A simple method was developed for synthesizing α,α'-dinaphthylmethane from naphthalene and α,α'-dichlorodimethyl ester in a medium of nitrobenzene in the presence of $AlCl_3$.

## LITERATURE CITED

[1] V. S. Etlis, G. A. Razuvaev, J. Gen. Chem. 27, 3092 (1957).*

[2] Dict. Org. Compounds (1949).**

[3] K. Dziewonski, S. Dziecielewski, Bull. Acad. Polon. Sciences Letters Series A, 1927, 273; Zbl. 1928, I, 57.

[4] G. A. Razuvaev, V. S. Etlis, J. Gen. Chem. 25, 1711 (1955).*

[5] J. Schmidlin, P. Massini, Ber. 42, 2381 (1909); A. Tschitschibabin, Ber. 44, 443 (1911).

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* Original Russian pagination. See C. B. Translation.

** In Russian.

# TRIAROXYPHOSPHAZOACYLS

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Triaroxyphosphazoacyls of the type of $RCON{=}P(OR')_3$ are similar in formula and nature to the readily accessible and fairly well studied triaroxyphosphazo compounds of the type of $RSO_2N{=}P(OR')_3$ [1]. Nevertheless there are also profound differences between them due to the fundamental differences in the chemical characters of the $RCO-$ and $RSO_2-$ residues. The similarity between triaroxyphosphazoacyls and triaroxyphosphazosulfo compounds is manifested in a series of general chemical properties and also in the fact that they can be prepared by similar reaction schemes:

$$RCON{=}PCl_3 + 3NaOR' \rightarrow 3NaCl + RCON = P(OR')_3 \qquad (I)$$

$$RSO_2N{=}PCl_3 + 3NaOR' \rightarrow 3NaCl + RSO_2N{=}P(OR')_3 \qquad (II)$$

Their behavior on heating and hydrolysis reveals the principal fundamental differences in the chemical nature of triaroxyphosphazoacyls (I) and triaroxyphosphazosulfo compounds (II). Depending upon the nature of the radical R, compounds (I) more or less easily split off the corresponding triester of phosphoric acid when heated and gave nitriles (compare [2]) according to the equation

$$RCON{=}P(OR')_3 \rightarrow OP(OR')_3 + RCN \qquad (III)$$

Reaction (III) goes quickly at room temperature in presence of hydrogen chloride as catalyst (compare [3]). Compounds (II) are remarkably resistant to heating, and hydrogen chloride has no action on them. No case has hitherto been known of thermal cleavage of compounds (II) by a mechanism similar to the cleavage of (III), although such a cleavage cannot be altogether excluded in principle. This difference is undoubtedly due to nitriles being thermodynamically favored and to compounds of the type of $RSO{\equiv}N$ being thermodynamically unfavored. It may be mentioned, however, that in one case a compound of this type (more correctly its trimer) could be obtained by thermal cleavage of the acid chloride of trichlorophosphazosulfuric acid [4].

Compounds (II) are easily saponified by caustic alkalies with formation of salts of the diesters of the corresponding alkyl- or arylsulfonamidophosphoric acids [5], but they are substantially not hydrolyzed by water in neutral solutions. No difficulties therefore arise in the preparation and isolation of compounds (II). Compounds (I) are hydrolyzed with amazing ease (compare [6]). When a bottle containing crystalline triphenoxyphosphazobenzoyl (IV) is opened, a waxy film quickly forms on the surface of the crystals and the substance absorbs moisture from the air and is quickly transformed into a semiliquid mixture of phenol and the diphenyl ester of benzoylamidophosphoric acid. Liquid triphenoxyphosphazo-p-nitrobenzene (VI) quickly turns cloudy in contact with atmospheric moisture and soon deposits crystals of the corresponding diester. Boiling of all of substances (I) with 96% alcohol substantially hydrolyzes them to the diesters of the acylamidophosphoric acids. The preparation, isolation and purification of triaroxyphosphazoacyls is therefore associated with great experimental difficulties, and arrangements must be made to exclude atmospheric moisture. This marked difference is evidently due to the fact that hydrolysis of triaroxyphosphazoacyls (I) in alkaline solutions involves participation of carbon and oxygen atoms of the carboxyl group, thus increasing the positive charge of the phosphorus atom in accordance with the equation

TABLE 1

Triaroxyphosphazoacyls $ArCON{=}P(OAr')_3$ (I)

| Substance no. | Ar | Ar′ | Crystallization medium, form of crystals | Yield (%) | Melting point | Found (%) N | Gross formula | Calculated (%) N |
|---|---|---|---|---|---|---|---|---|
| IV | $C_6H_5$ | $C_6H_5$ | Ligroine, stout prisms | 80.3 | 74—76° | 3.20 | $C_{25}H_{20}O_4NP$ | 3.26 |
| V | $\alpha$-$C_{10}H_7$ | $C_6H_5$ | Ligroine, prisms | 82.0 | 60—63 | 2.99 | $C_{29}H_{22}O_4NP$ | 2.91 |
| VI | p-$NO_2C_6H_4$ | $C_6H_5$ | Liquid | 83.9 | — | 5.84 | $C_{25}H_{19}O_6N_2P$ | 5.91 |
| VII | 3,5-$(NO_2)_2C_6H_3$ | $C_6H_5$ | Ligroine, aggregates of prisms | 78.5 | 87—89 | 8.36 | $C_{25}H_{16}O_8N_3P$ | 8.10 |
| VIII | 2-Cl-4-$NO_2C_6H_3$ | $C_6H_5$ | Liquid | 79.1 | — | 5.41 | $C_{25}H_{18}O_6N_2PCl$ | 5.52 |
| IX | p-$ClC_6H_4$ | $\alpha$-$C_{10}H_7$ | Benzene + ligroine, prisms | 73.4 | 156—158 | 2.30 | $C_{37}H_{25}O_4NPCl$ | 2.29 |
| X | 3,5-$(NO_2)_2C_6H_3$ | p-$ClC_6H_4$ | Benzene, rhombohedra | 82.0 | 150—152 | 7.01 | $C_{25}H_{15}O_8N_3PCl_3$ | 6.75 |
| XI | p-$NO_2C_6H_4$ | o-$NO_2C_6H_4$ | Benzene + ligroine, light-yellow needles | 79.7 | 130—133 | 11.66 | $C_{25}H_{16}O_{12}N_5P$ | 11.49 |
| XII | 3,5-$(NO_2)_2C_6H_3$ | $CH_3$ | $CCl_4$, prisms | 84.0 | 68—70 | 12.81 | $C_{10}H_{12}O_8N_3P$ | 12.61 |

TABLE 2

Diesters of Acylamidophosphoric Acids $ArCONHPO(OAr')_2$ (XIII)

| Ar | Ar′ | Form of crystals | Yield (%) | Melting point | Found |  | Gross formula | Calculated* N (%) |
|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  | N (%) | calc. |  |  |
| $C_6H_5$ | $C_6H_5$ | Prisms | 96.1 | 147—149° | see [6] | — | — | — |
| $\alpha$-$C_{10}H_7$ | $C_6H_5$ | Plates | 97.0 | 127—129 | 3.59 | 1.00 | $C_{23}H_{18}O_4NP$ | 3.48 |
| p-$NO_2C_6H_4$ | $C_6H_5$ | Prisms | 97.0 | 151—152 | see [6] | — | — | — |
| 3,5-$(NO_2)_2C_6H_3$ | $C_6H_5$ | Prisms | 99.0 | 197—199 | 9.51 | 0.97 | $C_{19}H_{14}O_8N_3P$ | 9.50 |
| 2-Cl-4-$NO_2C_6H_3$ | $C_6H_5$ | Prisms | 93.4 | 107—109 | 6.50 | 0.98 | $C_{19}H_{14}O_6N_2PCl$ | 6.48 |
| p-$ClC_6H_4$ | $\alpha$-$C_{10}H_7$ | Prisms | 94.9 | 165—167 | 3.04 | 1.00 | $C_{27}H_{19}O_4NPCl$ | 2.88 |
| 3,5-$(NO_2)_2C_6H_3$ | p-$ClC_6H_4$ | Needles | 98.1 | 216—217 | 8.42 | 0.98 | $C_{19}H_{12}O_8N_3PCl_2$ | 8.36 |
| p-$NO_2C_6H_4$ | o-$NO_2C_6H_4$ | Light-yellow prisms | 95.3 | 178—179 | [6] | — | — | — |
| 3,5-$(NO_2)_2C_6H_3$ | $CH_3$ | Needles | 98.1 | 189—191 | 13.40 | 1.01 | $C_9H_{10}O_8N_3P$ | 13.15 |

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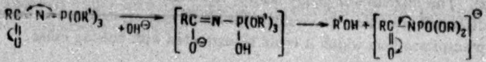
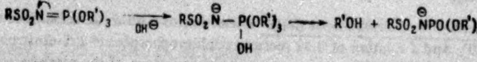
*Equivalent calc.: 1.0.



$$RC(=O)N=P(OR')_3 \xrightarrow[+OH^{\ominus}]{} \left[ \begin{array}{c} RC=N-P(OR')_3 \\ \;\;|\qquad\quad\;\; | \\ O^{\ominus}\qquad OH \end{array} \right] \longrightarrow R'OH + \left[ RC(=O)NPO(OR)_2 \right]^{\ominus}$$

In the main only the nitrogen and phosphorus atoms participate in the mechanism of hydrolysis of triaroxyphosphazosulfo compounds in alkaline solutions:



$$RSO_2N=P(OR')_3 \xrightarrow[OH^{\ominus}]{} RSO_2\overset{\ominus}{N}-\underset{OH}{\underset{|}{P}}(OR')_3 \longrightarrow R'OH + RSO_2\overset{\ominus}{N}PO(OR')_2,$$

for the sulfur and oxygen atoms of the sulfo group cannot appreciably increase the positive charge of the phosphorus atom since the $S^{VI}=N$ bond is extraordinarily unfavored (compounds containing the $S^{VI}=N$ bond are nearly unknown), and therefore conjugation between the $O=S^{VI}$ and $N=P$ bonds is improbable.

Triphenoxyphosphazobenzoyl (IV) and triphenoxyphosphazo-p-nitrobenzoyl (VI) were also synthesized by the action of the corresponding azides on triphenyl phosphite (compare [7]) according to the equation:

$$ArCON_3 + P(OC_6H_5)_3 \rightarrow [ArCON=N-N=P(OC_6H_5)_3] \rightarrow N_2 + ArCON=P(OC_6H_5)_3$$

Compounds (IV) and (VI) prepared by this route were found to be identical with the products obtained from trichlorophosphazoacyls and sodium arylates, so that their structure is established. The remaining properties of the triaroxyphosphazoacyls are presented in Table 1 and in the experimental part.

## EXPERIMENTAL

All of the operations from start to end of the synthesis of triaroxyphosphazoacyls must be performed as far as possible under conditions excluding reaction with moisture of the air. The nature of the acyl radical in the aromatic ring evidently has little influence on the rate of hydrolysis. The nature of the ester radicals plays a much more important part. Triphenoxyphosphazoacyls (IV-VIII) are especially easily hydrolyzed; compound (X) is hydrolyzed with slightly more difficulty and compound (XI) with appreciably more difficulty; but even (XI) is rapidly transformed into the corresponding diester when kept in 96% alcohol in the air. The exceptional ease of hydrolysis of compounds (I) enabled the diesters of aromatic acylamidophosphoric acids to be prepared from trichlorophosphazoacyls and sodium arylates in good yields without isolation of compounds (I) [6].

Triphenoxyphosphazobenzoyl (IV). To a solution of 0.025 mole of trichlorophosphazobenzoyl in 40 ml of dioxane was added rapidly (with vigorous stirring) a suspension of 0.075 mole of finely pulverized and thoroughly dried sodium phenate in 50 ml of dioxane. A fair amount of heat was liberated and the reaction was completed in 4-5 minutes. The precipitated sodium chloride was removed by centrifuging (in closed vessels) and the dioxane was distilled off in vacuo. The residue was a colorless liquid which crystallized completely at 0° after 2-3 hours. The product (IV) was purified by recrystallization from ligroine.

Compounds (V-VIII) were similarly prepared. Liquid (VI) and (VIII) were purified by reprecipitation from benzene or dioxane solutions by addition of ligroine.

Tri-α-naphthoxyphosphazo-p-chlorobenzoyl (IX). 0.03 g-atom of sodium was added to a solution of 0.03 mole of α-naphthol in 70 ml of ether. After the whole of the sodium had dissolved, a solution of 0.01 mole of trichlorophosphazo-p-chlorobenzoyl in 40 ml of ether was slowly stirred in. The reaction went with evolution of heat. After the whole of the chloride had been added, stirring was continued for another 10-15 minutes. The mixture was then heated to the boil and the sodium chloride filtered off. On cooling, the solution deposited (IX) as fine prisms. Part of the (IX) remained in the precipitated sodium chloride and could be extracted by boiling with ether.

Tri-p-chlorotriphenoxyphosphazo-3,5-dinitrobenzoyl (X). To a mixture of 30 ml of ether, 20 ml of benzene and 0.045 mole of sodium p-chlorophenate was gradually added a solution of 0.015 mole of trichlorophosphazo-3,5-dinitrobenzoyl in 40 ml of benzene with continuous stirring. The reaction went with fairly considerable release of heat, and the reaction mixture immediately turned brown, but the color disappeared at the end of the reaction (10-15 minutes). The mixture was gently heated, the sodium chloride was separated by centrifuging, and the solvent was distilled off in vacuo. The residue was an oil that crystallized at once. Part of (X) remained in the sodium chloride precipitate from which it could be extracted with boiling ether.

Tri-o-nitrotriphenoxy-p-nitrobenzoyl (XI). A mixture of 0.02 mole of trichlorophosphazo-p-nitrobenzoyl, 0.062 mole of pulverized sodium o-nitrophenate and 50 ml of benzene was refluxed for 1 hour, the sodium chloride and excess of sodium nitrophenate were suction-filtered, and the benzene was distilled off in vacuo. The residue was crystalline (XI).

Trimethoxyphosphazo-3,5-dinitrobenzoyl (XII). A solution of 0.06 mole of sodium methoxide in 40 ml of methanol was cooled to 0°, and a solution of 0.02 mole of trichlorophosphazo-3,5-dinitrobenzoyl in 50 ml of benzene was added with vigorous stirring at such a rate that the temperature of the mixture was maintained at 0 to +5°. The reaction mixture was then heated to the boil, the sodium chloride was separated by centrifuging and the solvent was distilled off in vacuo. 1 to 2 ml of ligroine was added to the liquid residue. After 2-3 hours' standing at 0°, compound (XII) crystallized completely.

All of compounds (I) are readily soluble in dioxane, poorly soluble in cold ligroine and very much more soluble at the boil. Compounds (IX) and (XI) are sparingly soluble in cold ether; all the others are easily soluble. The majority of compounds (I) crystallize nicely from ligroine or from a mixture of benzene and ligroine; (XII) crystallizes from $CCl_4$.

Cleavage of triaroxyphosphazoacyls according to equation (III) easily takes place on heating or at room temperature in presence of hydrogen chloride. 0.05 mole of (IV) was placed in a small Claisen flask, and dry hydrogen chloride was charged in. After 24 hours the crystalline (IV) had completely liquefied. The benzonitrile was distilled off in a vacuum of about 1 mm (26-37°) and redistilled without vacuum in a small column; b. p. 188.5-189.5°; yield 86%. It was identified by its melting point, specific gravity and refractive index. The residue after the first distillation of benzonitrile was recrystallized from alcohol to give triphenyl phosphate (yield 82%) with m. p. 49-50°; it was identified in a mixed melting test.

0.05 mole of (IV) was distilled in vacuo and the following fractions were collected: 74-90° (13 mm, benzonitrile); 90-240° (intermediate, 2.5 g); 240-244° (10 mm, triphenyl phosphate). Redistillation of the first fraction gave 89.5% of pure benzonitrile (b. p. 188.5-189.5°); redistillation of the last fraction gave 68.5% of pure triphenyl phosphate (m. p. 49-50°). All of the other compounds (I) were cleaved in similar fashion.

Hydrolysis of triaroxyphosphazoacyls to diesters of acylamidophosphoric acids (XIII). Hydrolysis was effected by mixing compounds (I) with water or by exposing to the air in a thin layer. (XIII) was most conveniently prepared by boiling compounds (I) with an aqueous alcoholic solution of sodium hydroxide or with 96% alcohol. Table 2 contains the yields of (XIII) obtained by boiling (I) (0.01 mole) with 50 ml of 96% alcohol for 1 hour. Compounds (XIII) were purified by recrystallization from aqueous alcohol.

The newly prepared compounds (XIII), like those previously synthesized [6], are acidic crystalline substances that titrate with phenolphthalein like monobasic acids. They are very sparingly soluble in hot water (the dimethyl ester is very much more soluble) and ether, easily soluble in benzene, acetone, dioxane; they can be recrystallized from alcohol.

Reaction of benzoyl azide with triphenyl phosphite. A mixture of 0.01 mole of benzoyl azide, 0.01 mole of triphenyl phosphite and 15 ml of ether was refluxed for 2 hours; the ether was driven off on a water bath. A thermometer was inserted in the residual liquid which was slowly heated. Nitrogen started to come off at 80°; a violent reaction commenced at 110°, and then the external heating was stopped. Due to the heat of reaction the temperature of the liquid rose to 160°. After the liquid had cooled, 10 ml of ligroine and a seed crystal of (IV) were added. Crystals quickly deposited and were suction-filtered and washed with ligroine. The triphenoxyphosphazobenzoyl obtained in this fashion was identical with the product synthesized from trichlorophosphazobenzoyl and sodium phenate; yield 32.7%.

Liquid (VI) was similarly prepared in 99.2% yield from p-nitrobenzoyl azide and triphenyl phosphite. It was identified by conversion to the diphenyl ester of p-nitrobenzoylamidophosphoric acid by boiling with 96% alcohol. Yield of diester 77.8%, m. p. 151-152°; it does not give a depression of melting point with the diester prepared from compound (VI) synthesized from trichlorophosphazo-p-nitrobenzoyl and sodium phenate.

## SUMMARY

Triaroxyphosphazoacyls of the aromatic series and trimethoxyphosphazo-3,5-dinitrobenzoyl were prepared; some of their chemical properties were studied.

## LITERATURE CITED

[1] A. V. Kirsanov and V. I. Shevchenko, J. Gen. Chem. 24, 474 (1954);* 26, 74, 250, 504 (1956).*

[2] A. V. Kirsanov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1954, 646.*

[3] A. V. Kirsanov and R. G. Makitra, J. Gen. Chem. 26, 907 (1956).*

[4] A. V. Kirsanov, J. Gen. Chem. 22, 81 (1952).*

[5] A. V. Kirsanov and V. I. Shevchenko, J. Gen. Chem. 24, 1980 (1954).*

[6] A. V. Kirsanov and R. G. Makitra, J. Gen. Chem. 27, 450 (1957).*

[7] H. Staudinger, J. Meyer, Helv. chim. Acta 4, 861 (1921).

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* Original Russian pagination. See C. B. Translation.

# NITROGEN COMPOUNDS OF PHENYLATED DERIVATIVES OF THIOPHENE. I.

V. N. Ivanova

Phenylated thiophenes, not to mention their nitrogen derivatives, form a very neglected branch of thiophene chemistry. The literature only contains short reports of the synthesis of a few phenylthiophenes [1]. Tetraphenylthiophene is an exception in that it has been studied in detail by Diltey and Graef [2].

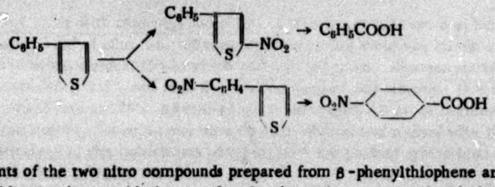
We chose monosubstituted α- and β-phenylthiophenes as compounds for study. They were synthesized by the method of A. S. Broun and M. G. Voronkov [3]. The nitration reaction was carried out in order to obtain nitrogen-containing derivatives of α- and β-phenylthiophenes. The usual methods of nitration did not give satisfactory results. Only when using copper nitrate as the nitrating agent in a medium of acetic anhydride (procedure of N. I. Putokhin [4]) did we observe a quiet course of the reaction with formation of nitro products in good yields (about 80%).

Nitration of β-phenylthiophene gave an adequately homogeneous crystalline product with a yellow color; m. p. 137-140°. The analysis corresponded to a mononitro compound of β-phenylthiophene.

Nitration of α-phenylthiophene led to two products. One of them (yield 75-80% of the total) consisted of golden-yellow crystals (needles) with m. p. 123-124°. The second nitro compound (yield 25-20%*)consisted of silvery yellow leaflets with m. p. 98-100°. In both cases the analyses corresponded to mononitro compounds of α-phenylthiophene.

It was necessary to elucidate the structure of these nitro compounds which had not been described in the literature. Oxidation was at first attempted with 5% potassium permanganate solution which was added in the theoretically calculated quantity. This procedure led, however, to complete decomposition of the molecule of the nitro compound (both the benzene and the thiophene rings broke down). More satisfactory oxidation conditions were established in a series of experiments. It was found necessary to introduce the oxidant in small portions and in low concentration (1% $KMnO_4$ solution) in quantity not exceeding 45-50% of the theoretical. Under these conditions the oxidation went very slowly and a proportion of the nitro compound (about 40%) was not oxidized.

Oxidation of nitro-β-phenylthiophene gave two substances. One of these (about 70% of the total yield) was benzoic acid (identified by conversion to benzanilide). The second substance (about 30% of the total yield) was a finely crystalline powder with m. p. 237° (after sublimation). Judging by the analysis and melting point, the substance is p-nitrobenzoic acid. The isolation of two oxidation products — benzoic acid and p-nitrobenzoic acid — indicates that nitration of β-phenylthiophene goes in two directions:



The melting points of the two nitro compounds prepared from β-phenylthiophene are very similar. The other compound that did not undergo oxidation was found to be a nitro compound with the nitro group in the thiophene ring.

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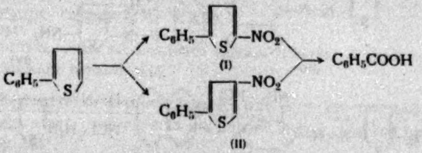
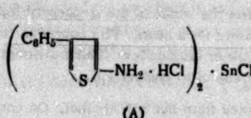
* As in original — Publisher's note.

The structure of the nitro compounds of α -phenylthiophene was studied under the same conditions as for the nitro compounds of β -phenylthiophene. The product of oxidation of each of the two nitro derivatives of α -phenylthiophene was benzoic acid (identified as benzanilide). Nitration of α -phenylthiophene therefore also proceeds in two directions but in this case the nitro group always enters the thiophene ring. Taking into account the greater reactivity of the α -hydrogen atoms, the main product of nitration (m. p. 123-124°) must evidently be assigned the formula of α'-nitro-α-phenylthiophene (I). For the second product the formula of β'-nitro-α-phenylthiophene (II) is more probable. The transformations may therefore be represented as follows:



The nitration reaction revealed a slight difference in the behavior of α- and β -phenylthiophenes. β -phenylthiophene gives a product with the nitro group in the benzene ring and one with the nitro group in the thiophene ring, whereas nitration of α-phenylthiophene gives substances with the nitro group only in the thiophene ring.

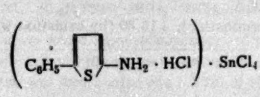
Reduction of the corresponding nitro compounds gave amino derivatives of α- and β -phenylthiophenes. The amines were isolated in the form of nicely crystallizing complex salts with tin chloride. Analysis of the complex salt of the amine prepared from a mixture of the nitro compounds of β -phenylthiophene corresponds to formula (A)



(A)

In proposing the above formula (A) we were guided by the fact that the formation of a complex salt with tin chloride is characteristic only of amines of thiophene but not of amines of benzene. We were unable to detect an amine in which the amino group was in the benzene ring. All attempts to isolate the free amine or its hydrochloride were unsuccessful, apparently due to the great instability of these substances.

Reduction of α'-nitro-α-phenylthiophene gave a complex salt of an amine with tin chloride whose analysis corresponds to formula (B)

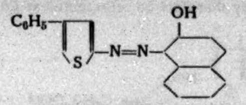


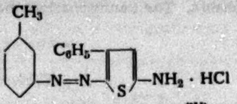
(B)

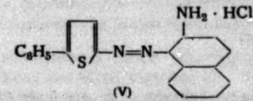
It was previously shown [5] that amines of thiophene in the form of their complex salts with tin chloride can be diazotized to give azo dyes. We also subjected the complexes of amines of α- and β -phenylthiophenes with tin salts to diazotization. Later it was shown that the diazo compounds from amines of α- and β -phenylthiophenes readily enter into the azo-coupling reaction with various aromatic amines, naphthols and their derivatives to form azo dyes. In this manner we obtained two dyes by coupling the diazotized complex salt of α'-amino-β -phenylthiophene in one case with β -naphthol (the dye forms dark-brown crystals) and in the other case with β -naphthylamine (brown, crystalline powder).

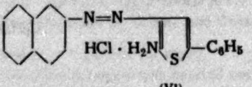
In addition we prepared dyes in which the azo component was the complex salt of α'-amino-β -phenylthiophene. In this case the yield of dye was considerably reduced. Again we obtained two dyes. Diazotized β -naphthylamine was coupled in one case with the complex salt of α'-amino-β -phenylthiophene (the resulting crystalline, cherry-red dye possessed indicator properties). In the other case diazotized m-toluidine was coupled with the complex salt of α'-amino-β-phenylthiophene (the dye was dark-red; it satisfactorily dyed wool and silk but was less satisfactory on cotton).

In similar fashion α'-amino-α-phenylthiophene was the starting substance for two azo dyes: the first was obtained by coupling diazotized α'-amino-α-phenylthiophene with β-naphthylamine (brown crystalline dye); the second by coupling diazotized β-naphthylamine with the complex salt of α'-amino-α-phenylthiophene (the dye formed dark cherry-red crystals). The formulas of the prepared dyes are given below:


(III)


(IV)


(V)


(VI)

## EXPERIMENTAL

I. Nitration of α-phenylthiophene. 2.25 g of copper nitrate and 15 ml of acetic anhydride were placed in a two-necked flask fitted with a thermometer extending to the bottom and a dropping funnel. The flask was cooled to 8-10° with iced water. A solution of 1.5 g of α-phenylthiophene in 15 ml of acetic anhydride was then run in portionwise from the dropping funnel. Addition of each portion caused the temperature to rise 2-4°. Nitration was performed at 10-12°. After the whole of the α-phenylthiophene solution had been added, the reaction mass was left at room temperature for 2 hours. The copper salts were then filtered under suction, and the filtrate was quickly treated with snow or crushed ice. This treatment caused an oil to separate which crystallized after 10-12 hours. Yield of crude nitro product 1.5 g.

The nitro product was recrystallized from hot 90% alcohol. On cooling, crystals came down in the form of golden needles with m. p. 121°; weight 0.825 g or 75% of the total yield of nitro compounds (substance 1); the crystals were quickly filtered.

More crystals came down from the mother liquor; these were silvery yellow leaflets, m. p. 95-97°, weight 0.275 g or 25% of the total yield (substance 2).

After recrystallization, substance 1 had m. p. 123-124°, and substance 2 had m. p. 98-100°.

Analysis of Substance 1

Found %: N 6.81 (Kjeldahl determination); S 15.80 (by oxidation with 5% $KMnO_4$). $C_{10}H_7O_2NS$. Calculated %: N 6.82; S 15.60.

Analysis of Substance 2

Found %: N 6.93; S 15.53. $C_{10}H_7O_2NS$. Calculated %: N 6.82; S 15.60.

II. Nitration of β-phenylthiophene. The procedure was similar to that with α-phenylthiophene. Reaction components were 1.8 g of copper nitrate in 10 ml of acetic anhydride, and 1.0 g of β-phenylthiophene in 10 ml of acetic anhydride. Yield of nitro derivative 0.8 g (62%). After recrystallization from 80% alcohol the product had m. p. 137-140°.

Found %: N 6.64; S 15.45. $C_{10}H_7O_2NS$. Calculated %: N 6.82; S 15.60.

III. Oxidation of nitro compounds of α- and β-phenylthiophenes. 1. Oxidation of nitro derivatives of β-phenylthiophene. 1 g of nitro compound and 100 ml of 1% potassium permanganate solution were placed in a 500 ml round-bottomed flask fitted with a reflux condenser. The flask was heated on a water bath. After 24 hours, the solution had lost its color; another 100 ml of 1% potassium permanganate solution was added, and heating on the water bath was continued. After 4-5 days, the solution was again colorless. A final 100 ml of 1% potassium permanganate solution was added. In this manner, 50% of the theoretical quantity of potassium permanganate for complete oxidation of the thiophene had been added. After the solution had again become colorless, (9-days' heating on the water bath), the precipitated $MnO_2$ was filtered off, and the filtrate was evaporated and acidified with hydrochloric acid (d 1.19). A fine, heavy, cream-colored precipitate came down; m. p. 189-192°; weight 0.038 g (substance 1). The acid filtrate from substance 1 was evaporated; on cooling it deposited light, white crystals with m. p. 120°; weight 0.1 g (substance 2).

Substance 1 sublimes; after sublimation it has m. p. 237°. A qualitative test reveals absence of nitrogen.

Found %: N 8.26. $C_7H_5O_4N$. Calculated %: N 8.38.

Substance 2 readily sublimes. After sublimation it melts at 121-122°; it forms benzanilide with m. p. 158-159°. The substance is therefore benzoic acid.

2. Oxidation of nitro derivatives of α-phenylthiophene with m. p. 123-124° and m. p. 98-100° was performed in similar fashion to the above. Benzoic acid was isolated in both cases and identified as benzanilide with m. p. 158-160° and m. p. 158°.

IV. Reduction of nitro derivatives of α- and β-phenylthiophenes. 1. Reduction of α'-nitro-α-phenylthiophene. Into a 100 ml round-bottomed flask, equipped with a reflux condenser, were charged 0.8 g of the nitro derivative and 40 ml of tin chloride solution [16.2 g of $SnCl_2$, 57 ml of HCl (d 1.19) and 15 ml of $H_2O$]. After being heated on an air bath (60-70°) for 2 hours, the orange solution was decanted from the dark residue of unreacted nitro compound. A crumbly crystalline precipitate with a light-sandy color at once came down from the filtrate. Another 15 ml of the above solution of tin chloride was added to the residue in the flask, and the latter was again heated for 1-1.5 hours. The orange solution was again decanted from undissolved residue, and the latter was again treated with 10 ml of the tin chloride and again heated for about an hour. This operation was repeated once again. Light-sand colored crystals also came down from the decanted liquids. The four filtrates were combined and the product of reduction was filtered off; yield 0.7 g.

Found %: N 3.10; S 6.86; Sn 25.26 (by Kocheshkov's method). $(C_{10}H_7SNH_2 \cdot HCl) \cdot SnCl_4$. Calculated %: N 2.96; S 6.77; Sn 25.14.

2. Reduction of the nitro compound of β-phenylthiophene. 1 g of nitro compound and 50 ml of solution of stannous chloride in hydrochloric acid [16.2 g $SnCl_2$, 57 ml HCl (d 1.19) and 15 ml $H_2O$] were placed in a round-bottomed flask of 100 ml capacity. The flask (to which a reflux condenser was attached) was heated on an air bath without the contents being brought to the boil. Heating was continued until the whole of the nitro compound had gone into solution (small traces of blackened nitro compound remained), which usually occurred after 2-2.5 hours. The hot solution was filtered and the filtrate left in a cold place. Orange-red crystals of reduction product appeared at the bottom of the flask after 24 hours; m. p. 178-180° (in a sealed capillary).

Found %: N 3.95; S 9.24; Sn 17.21. $(C_{10}H_7SNH_2 \cdot HCl)_2 \cdot SnCl_4$. Calculated %: N 4.07; S 9.37; Sn 17.37.

V. Diazotization of the amines of α- and β-phenylthiophenes and preparation of azo dyes. 1. Diazotization of α'-amino-α-phenylthiophene. 0.2 g of the complex tin salt of α'-amino-α-phenylthiophene was dissolved by heating in alcohol; the solution was then cooled and 0.2 ml of HCl (d 1.19) was added. A solution of 0.04 g of $NaNO_2$ in 2-3 ml of water was run dropwise with constant stirring into the solution of the complex salt (cooled to 0-5°) at such a rate that the temperature did not rise above +5°. Completion of the diazotization reaction was indicated by the blue color of starch-iodide paper. After the $NaNO_2$ solution had been added, the diazo solution was kept for half an hour in an ice bath; after filtration, it was used for the azo-coupling reaction.

2. Preparation of azo dyes, derivatives of α'-amino-α-phenylthiophene. a) Diazo solution from 0.2 g of the complex salt of α'-amino-α-phenylthiophene (prepared as above) was gradually run with stirring and cooling (5-8°) into a hydrochloric acid solution of β-naphthylamine (0.07 g of β-naphthylamine was dissolved in 3-4 ml of alcohol by heating; after cooling, 0.3 ml of HCl, d 1.19, was added). The solution at first turned dark cherry-red; addition of saturated NaCl solution brought down a flaky, brown precipitate of dye (V). Yield 0.14 g.

Found %: S 8.58. $C_{20}H_{16}N_3SCl$. Calculated %: S 8.76.

b) 0.1 g of β-naphthylamine was dissolved in aqueous alcohol; 0.2-0.4 ml of HCl (d 1.19) was added. The solution was cooled to 3-5° and dropwise addition was made of $NaNO_2$ solution (0.03 g in 2 ml of water). The resulting diazo solution was filtered and run dropwise into a cooled alcoholic-acid solution of the complex salt of α'-amino-α-phenylthiophene (0.33 g of complex salt was dissolved in 3-4 ml of alcohol and 0.3 ml of HCl, d 1.19, was added). A dark cherry-red dye (VI) came down. Yield of dye 0.24 g.

Found %: S 8.60. $C_{20}H_{16}N_3SCl$. Calculated %: S 8.76.

3. Diazotization of α'-amino-β-phenylthiophene. 0.5 g of the complex salt of α'-amino-β-phenylthiophene was dissolved by heating in 5 ml of alcohol; to the stirred and cooled (0-5°) solution was gradually added (dropwise) a solution of $NaNO_2$ (0.112 g in 3 ml of water). The temperature was not allowed to rise above +5°. Development of a blue color on starch-iodide paper indicated the completion of diazotization. After filtration, the diazo solution was used for the azo-coupling reaction.

4. Preparation of azo dyes, derivatives of α'-amino-β-phenylthiophene. a) Diazo solution from 0.5 g of complex salt of α'-amino-β-phenylthiophene (for preparation see above) was gradually poured with stirring and cooling (5-8°) into an alkaline solution of β-naphthol (0.25 g of β-naphthol in 5 ml of 10% NaOH). The solution at first turned cherry to violet in color, and then deposited dye (III). Yield of dye 0.1 g.

Found %: S 8.94. $C_{20}H_{14}ON_2S$. Calculated %: S 9.09.

b) 0.33 g of m-toluidine was dissolved in 3 ml of alcohol; 1 ml of HCl (d 1.19) was added and the solution was cooled to 3-4°. A solution of 0.23 g $NaNO_2$ in 1.5 ml of water was added dropwise to the cooled solution. Completion of diazotization was indicated by the development of a blue color on starch-iodide paper. With constant stirring and cooling, the m-toluidine diazo solution was added dropwise to an acid-alcoholic solution of the complex salt of α'-amino-β-phenylthiophene (1 g of complex salt was dissolved in 15 ml of alcohol with heating; after it had cooled, 0.5 ml of HCl, d 1.19, was added). Azo-coupling goes very quickly; the solution becomes blood-red and dye (IV) rapidly comes down. Yield of dye 0.63 g.

Found %: N 12.54; S 9.81. $C_{17}O_{16}N_3SCl$. Calculated %: N 12.74; S 9.71.

In conclusion we extend our profound thanks to N. I. Putokhin for valuable advice.

## SUMMARY

1. The nitration of α- and β-phenylthiophenes was studied. It was found that in both cases the reaction goes in two directions with formation of mononitro compounds. We synthesized α'-nitro-α-phenylthiophene, β'-nitro-α-phenylthiophene, α'-nitro-β-phenylthiophene, and (p-nitro-β-phenyl)-thiophene.

2. α'-Amino-α-phenylthiophene and α'-amino-β-phenylthiophene were synthesized in the form of complex salts with stannic chloride.

3. It was shown that in the form of complex salts with tin chloride, the amines of α- and β-phenylthiophenes can undergo diazotization and azo-coupling reactions, and can also be utilized as azo components.

## LITERATURE CITED

[1] Kues, Paal, Ber. 19, 3141 (1886); Paal, Ber. 18, 367 (1885); Paal, Püschel, Ber. 20, 2557 (1887); F. Ia. Perveev and N. I. Kudriashova, J. Gen. Chem. 23, 1569 (1953);* A. S. Broun and M. G. Voronkov, Proc. Acad. Sci. USSR 59, 7 (1948).

[2] W. Diltey, E. Graef, J. pr. Ch. 151, 257 (1938).

[3] A. S. Broun and M. G. Voronkov, J. Gen. Chem. 17, 1162 (1947).

[4] N. I. Putokhin, Collection of Scientific Transactions of the Kuibyshev Industrial Institute part 5, 271 (1955).**

[5] N. I. Putokhin and V. I. Iakovlev, Collection of Scientific Transactions of the Kuibyshev Industrial Institute part 4, 175 (1953).**

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* Original Russian pagination. See C. B. Translation.

** In Russian.

# THE ABSORPTION SPECTRA OF α- AND β-PHENYLTHIOPHENES AND THEIR NITRO DERIVATIVES. II

V. N. Ivanova

Methods of analysis based on molecular spectra are now widely used. Special attention has been paid to the regularities in the absorption spectra of organic compounds. It was found [1] that selective absorption in a specific region of the spectrum is often associated with the presence of a specific atomic grouping. When the same grouping is present in another molecule which may belong to an entirely different class of compounds, the same characteristic absorption is exhibited but disguised to some extent by the neighboring groups.

We made use of the data of molecular spectra in order to obtain a fuller characterization of the nitro compounds of α- and β-phenylthiophenes that we had prepared [2] and also in order to compare the absorption curves of the different nitro compounds. Absorption curves were plotted for the following substances: α- and β-phenylthiophenes, α'-nitro-α-phenylthiophene (m. p. 123-124°), β'-nitro-α-phenylthiophene (m. p. 98-100°), and mixtures of the isomeric nitro derivatives of β-phenylthiophene and α'-nitro-β-phenylthiophene.

The curves of these compounds were compared with those of diphenyl and its mononitro derivatives. Comparison of the absorption curves of α- and β-phenylthiophenes with the absorption curve of their aromatic analog (diphenyl) leads to the conclusion that the general form of the absorption maxima of all of the three compounds is the same, but the replacement of benzene ring in diphenyl by a thiophene ring (in the formation of phenylthiophenes) causes the absorption maximum to be shifted towards longer wavelengths (Fig. 1). Diphenyl has $\lambda_{max}$ 2470 A, β-phenylthiophene has $\lambda_{max}$ 2600 A, while α-phenylthiophene has $\lambda_{max}$ 2850 A. The last value illustrates the stronger effect of the benzene ring in the α-position on the shift of the absorption maximum.

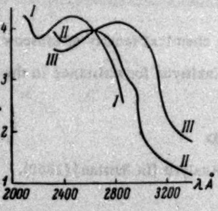


Fig. 1. Absorption spectra of diphenyl (I), β-phenylthiophene (II) and α-phenylthiophene (III).

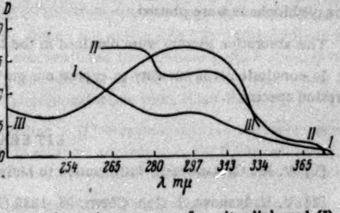
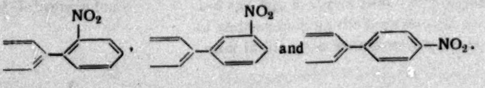


Fig. 2. Absorption spectra of o-nitrodiphenyl (I), m-nitrodiphenyl (II) and p-nitrodiphenyl (III).

Comparison of the absorption curves of o-, m- and p-nitro compounds of diphenyl reveals that the form of the curves varies in dependence on the position of the nitro group (Fig. 2).

Consequently in this case the absorption is caused by different atomic groupings, namely:



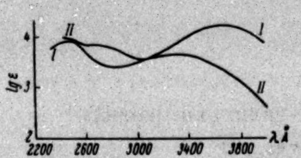


Fig. 3. Absorption spectra of α'-nitro-α-phenylthiophene (I) and β'-nitro-α-phenylthiophene (II).

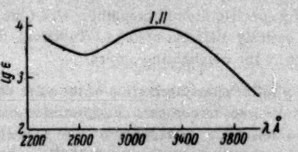
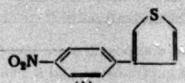


Fig. 4. Absorption spectra of a mixture of mononitro compounds of β-phenylthiophene (I) and α'-nitro-β-phenylthiophene (II). See text.

We observe a similar phenomenon on examination of the absorption curves of the isomeric nitro compounds of α-phenylthiophene (Fig. 3). There is no resemblance at all between the absorption curves of the two isomers. This is because the absorption is brought about by the nitro groupings in different positions (α- and β-) of the thiophene ring. A different picture is obtained when we plot the absorption spectra of nitro compounds of β-phenylthiophene. It was previously pointed out [2] that we had failed to separate the nitro compounds of β-phenylthiophene by crystallization. In one case the absorption measurements were made on an unresolved mixture of isomeric nitro compounds; in another case the sample was α'-nitro-β-phenylthiophene. It was found that both of the absorption curves have the same form and the same $\lambda_{min}$ of 2650 A and $\lambda_{max}$ of 3150-3200 A (Fig. 4). We can therefore conclude that one and the same substance is responsible for the spectral absorption curve in the two cases, namely α'-nitro-β-phenylthiophene. The absorption curve of the second substance in the mixture, present in insignificant quantity, could not be detected.



(A)

## SUMMARY

1. Absorption curves of α- and β-phenylthiophenes were plotted and found to be similar to the absorption curve of diphenyl.

2. The absorption spectra of α'-nitro-α-phenylthiophene, β'-nitro-α-phenylthiophene and α'-nitro-β-phenylthiophene were plotted.

The absorption spectra were obtained in the laboratory of the chemical faculty of Moscow State University.

In conclusion it is our duty to express our gratitude to L. A. Kazitsyna for assistance in the plotting of the absorption spectra.

## LITERATURE CITED

[1] V. M. Chulanovskii, Introduction to Molecular Spectral Analysis [in Russian] (1950).

[2] V. N. Ivanova, J. Gen. Chem. 26, 1232 (1956).*

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# THE ABSORPTION SPECTRA AND STRUCTURE OF SUBSTITUTED QUINOLINES SERVING AS STARTING SUBSTANCES FOR ANTIMALARIALS

## V. STRUCTURE AND TAUTOMERISM OF THE 2- AND 4-AMINOQUINOLINES

V. I. Bliznlukov and N. T. Solonskaia

Spectroscopic methods are undoubtedly valuable for clarification of the structure and tautomerism of 2- and 4-aminoquinolines, although the conclusions from different investigations are not always consistent. Steck and Ewing [1], for example, and Hearn, Morton and Simpson [2] consider these compounds to be tautomeric on the basis of a study of the ultraviolet spectra, whereas the spectral data of Angual and Werner [3] indicate the absence of tautomerism. A closer study of the spectrography of 2- and 4-aminoquinolines was carried out in the present work in solutions of hexane, ethanol, dioxane, chloroform and water, as well as in solutions of perchloric, sulfuric and hydrochloric acids and in alkaline solutions of sodium ethoxide. The compounds were investigated in the concentration range of $2 \cdot 10^{-2}$ to $2 \cdot 10^{-5}$ molar.

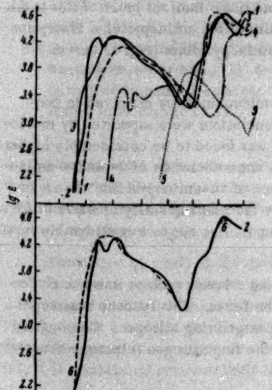

Fig. 1. Absorption spectra. 1) 4-aminoquinoline in dioxane; 2) 4-aminoquinoline in water; 3) 4-aminoquinoline in ethanol; 4) quinoline in ethanol; 5) 4-aminoquinoline in water (the spectrum is one tenth as intense); 6) 1-methyl-4-iminoquinoline in water.

2-Aminoquinoline was prepared by the action of sodium amide on quinoline [4] (m. p. 130°), while 4-aminoquinoline was prepared by the action of ammonia on 4-chloroquinoline in fused phenol in similar fashion to the preparation of 4-amino-7-chloroquinoline [5] or Akrikhin* [6], m. p. 155°. 1-Methyl-4-iminoquinoline was obtained by V. I. Konovalov from 4-aminoquinoline in a manner similar to the preparation of 10-methyl-9-iminoacridine [7,8]; it had m. p. 134° (with decomp.). 4-Acetylaminoquinoline was prepared by acetylation of 4-aminoquinoline with acetic anhydride [7]; m. p. 176°. Before use, the purified 2- and 4-aminoquinolines were recrystallized from benzene, the 1-methyl-4-iminoquinoline was recrystallized from absolute ether, and the 4-acetylaminoquinoline from ethanol.

According to [1] 4-aminoquinoline has three absorption bands in ethanol; according to [2] it has two bands. We found five bands in solutions in ethanol, dioxane and water.

According to [1] 2-aminoquinoline has two absorption bands in ethanol and alkali solution. We detected three absorption bands in solutions in ethanol, hexane, dioxane and chloroform.

In general appearance and arrangement, the bands of 2- and 4-aminoquinolines in organic solvents are similar to the spectra of unsubstituted quinoline. The bands of the latter are characteristic of benzene and pyridine (Fig. 1, curves 1-4 and Fig. 5, curves 1-5). This signifies that in molecules of aminoquinolines the benzene and aminopyridine rings interact in the same manner as the benzene and pyridine rings interact in unsubstituted quinoline [9,10]. On the basis of this similarity, we arbitrarily speak of the "benzene" and "pyridine" absorption bands of the isomeric aminoquinolines.

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* Transliteration of Russian – Publisher's note.

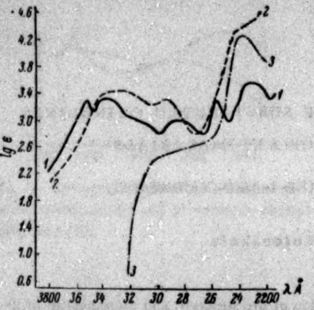


Fig. 2. Absorption spectra. 1) 1-methyl-4-iminoquinoline in hexane; 2) 1,4-naphthoquinone in absolute ethanol [25]; 3) 1,4-benzoquinone in hexane [26].

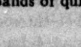
Under the influence of ionizing solvents such as water, or on formation of a salt at the ring nitrogen, a fourth band appears in the absorption spectra in the form of an inflection with $\lambda_{max}$ 2580 A and $\epsilon$ 50,000; at the same time the fine structure of the long-wave benzene band of 4-aminoquinoline becomes conspicuous (Fig. 1, curves 2 and 5; Fig. 3, curves 1-3). The band with $\lambda_{max}$ 2580 A becomes stronger in the spectrum of the 4-acetylaminoquinoline ion (Fig. 3, curves 4 and 7). Judging by its origin, the band with $\lambda_{max}$ 2580 A must be included among the bands formed by the conjugation of the $NH_2$ group with the ring and the ring nitrogen, just as in the case of 4-aminopyridine. For this reason the band in question is called the "p-aminopyridine" absorption band, but it is one tenth as strong as the corresponding band of 4-aminopyridine.

The spectra of the aqueous solution of 2-aminoquinoline or of its ion exhibit "o-aminopyridine" absorption bands of nearly the same intensity as the bands of 2-aminopyridine, which are superposed on the "benzene" spectrum of 2-aminoquinoline (Fig. 5, curves 3, 6, 7; Fig. 6, curves 1-4).

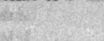
The influence of the amino group on the quinoline system in molecules of 2- and 4-aminoquinolines is reflected in activation of the benzene ring and in deactivation of the pyridine ring. Indirect proof of this is the increased intensity of their "benzene" absorption bands and weakened intensity of the aminopyridine absorption bands in comparison with the corresponding bands of quinoline or 2- and 4-aminopyridines (Fig. 1, curves 3-5 and Fig. 5, curves 3 and 7).

The absence of "aminopyridine" bands from the spectra of 2- and 4-aminoquinolines dissolved in nonionized solvents can be accounted for by association of molecules. These conclusions were supported by molecular weight determinations. The degree of association of 4-aminoquinoline was found to be considerably higher than that of 2-aminoquinoline. Even in solutions of the order of $10^{-3}$ molar, the association of 2- and 4-aminoquinolines does not disappear entirely. Indirect proof of this is the appearance of "o-aminopyridine" bands in the spectrum of the hexane-water solution of 2-aminoquinoline. Presumably the small quantity of water (0.07%) dissolved in the hexane dissociates the less associated molecules of 2-aminoquinoline but to a considerably smaller extent than in the case of 2-aminopyridine [11].

The associated molecules are dissociated under the influence of ionizing solvents such as water or on formation of a salt at the ring nitrogen, a positive charge being developed at the latter. This leads to rearrangement of the electronic density along the amino group toward the positively charged ring nitrogen. Conjugation is set up between the amino group, the $\pi$-electrons of the pyridine ring and the ring nitrogen (electron-accepting), just as in the cases of 2- and 4-aminopyridines [11] (I and II).



(I)



(II)

This interpretation is confirmed by the increased basicity of the ring nitrogen of 4-aminoquinoline in comparison with the basicity of quinoline [11].

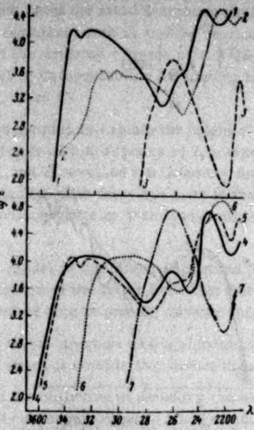


Fig. 3. Absorption spectra. 1) 4-aminoquinoline in ethanolic HCl (molar ratio 1:100); 2) 4-chloroquinoline in ethanolic HCl (molar ratio 1:100); 3) 4-aminopyridine in ethanolic HCl (molar ratio 1:100); 4) 4-acetylaminoquinoline in ethanolic HCl (molar ratio 1:100); 5) 4-acetylaminoquinoline in 5 M ethanolic HCl (after 30-minutes' heating on water bath); 6) 4-acetylaminoquinoline in neutral ethanol; 7) 4-aminopyridine in ethanolic HCl.

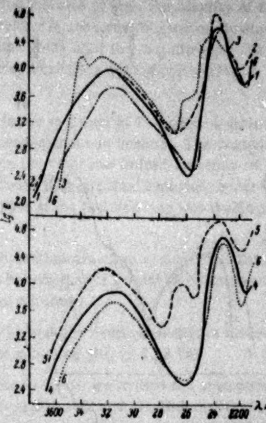


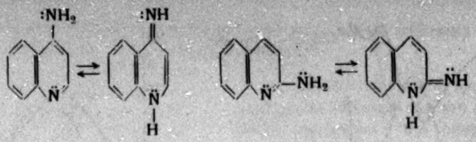
Fig. 4. Absorption spectra. 1) 4-aminoquinoline in concentrated sulfuric acid; 2) 4-aminoquinoline in 12 M perchloric acid; 3) 4-aminoquinoline in ethanolic HCl (molar ratio 1:100); 4) 4-acetylaminoquinoline in concentrated sulfuric acid; 5) 4-acetylaminoquinoline in 12 M perchloric acid; 6) quinoline in concentrated sulfuric acid.

The structure of the singly-charged 4-aminoquinoline ion has been frequently discussed [12-15]. None of the speculations about the addition of a proton to the ring nitrogen take into account, however, the possibility of interaction of the benzene ring with the aminopyridine ring and of conjugation of the amino group with the ring and the ring nitrogen.

Formation of a salt at the amino group and simultaneously at the ring nitrogen results in disappearance of the influence of these groups on the pyridine ring. The spectra of 2- and 4-aminoquinolines in concentrated sulfuric acid then become similar to the spectra of the unsubstituted quinolinium ion (Fig. 4, curves 1, 4, 6 and Fig. 6, curves 5 and 6). In solution in a weaker acid, however, such as 12 M perchloric acid, salt formation at the amino group of 4-aminoquinoline and 4-acetylaminoquinoline is incomplete, and a corresponding equilibrium is established between their singly-charged and doubly-charged ions (Fig. 4, curves 2, 5 and 6).

Absence of sulfonation on dissolution of 2- and 4-aminoquinolines in concentrated sulfuric acid was proved by observation of the spectra plotted after the sulfuric acid solutions had been diluted 5-fold (20% $H_2SO_4$ content). The resulting curves were identical with those obtained for a solution in 5 M ethanolic hydrogen chloride. No process other than salt formation therefore takes place in concentrated sulfuric acid.

The isomeric 2- and 4-aminoquinolines, which resemble the corresponding compounds of the pyridine series, are markedly different in chemical properties from their isomers in which the amino group is in position 3 of the pyridine ring or in the benzene ring. Thus, for example, 2- and 4-aminoquinolines are not diazotized under normal conditions [16-20]; they form two series of derivatives with alkyl halides [21, 22]; they do not give salts with 2 equivalents of hydrogen chloride, and they are the strongest bases [12]. The dual reactivity of 2- and 4-aminoquinolines and their other [23-25] special characteristics have been explained by tautomerism between the amino and imino forms:



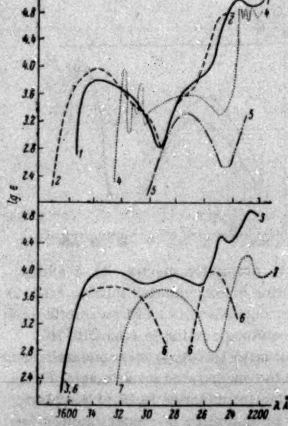


Fig. 5. Absorption spectra. 1) 2-aminoquinoline in hexane; 2) 2-aminoquinoline in ethanol; 3) 2-aminoquinoline in water; 4) 2-chloroquinoline in hexane; 5) pyridine in hexane (spectrum displaced 200 A toward the long waves); 6) 2-hydroxyacetophenone in ethanol [33]; 7) 2-aminopyridine in water.

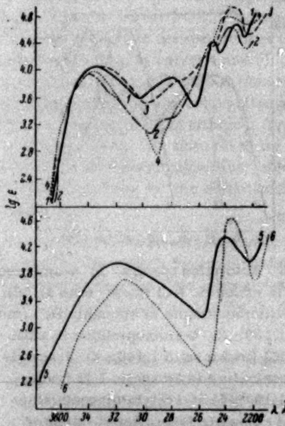
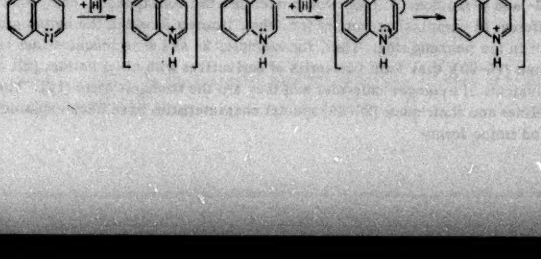


Fig. 6. Absorption spectra. 1) 2-aminoquinoline in ethanolic HCl (molar ratio 1:100); 2) 2-aminoquinoline in ethanolic HCl (molar ratio 1:0.1); 3) 2-aminoquinoline in ethanolic HCl (molar ratio 1:1); 4) 2-aminoquinoline in ethanol; 5) 2-aminoquinoline in concentrated sulfuric acid; 6) quinoline in concentrated sulfuric acid.

It is true that the spectrum of 4-aminoquinoline is hardly shifted when salt formation takes place at the ring nitrogen, in contrast to what happens in the case of 3-aminoquinoline. Moreover, 1-methyl-4-iminoquinoline gives a spectrum in water and in acid solutions which is identical with the spectrum of the 4-aminoquinolinium ion (Fig. 1, curves 6 and 2). This similarity between the absorption spectra of 4-aminoquinoline and 1-methyl-4-iminoquinoline could also have arisen if they had different structures but on condition that in the former (the amino form) the salt-forming center was the ring nitrogen, and that in the latter (the imino form) the salt-forming center was the nitrogen of the imino group.



In both cases the same 4-aminoquinolinium ion is formed, and this also governs the identity of the spectra of the two substances both in an acid medium and in ionizing solvents. In anhydrous hexane or dioxane, which do not bind the unshared electron pair of the nitrogen of the 4-imino group or of the ring nitrogen, the spectrum of 1-methyl-4-iminoquinoline has nothing in common with the spectrum of 4-aminoquinoline (Fig. 1, curve 2 and Fig. 2, curve 1).

We attempted to explain the origin of the absorption bands in the spectrum of 1-methyl-4-iminoquinoline by comparing it with the spectra of 1,4-naphthoquinone and 1,4-benzoquinone in hexane. The comparison (Fig. 2, curves 1 and 2) revealed a satisfactory similarity. Superposed on the "quinone-imine" spectrum of 1-methyl-4-iminoquinoline with three bands, as in the case of 1,4-benzoquinone [27], are the "benzene" bands as in the case of naphthoquinone or 4-aminoquinoline. This could only happen if the pyridine ring was lacking in aromatic character.

As a model of the tautomeric amino form we took 4-dimethylaminoquinoline; according to the literature [1] the spectrum of the latter resembles that of 4-aminoquinoline but not that of 1-methyl-4-iminoquinoline, when examined both in organic solvents and in acidic and alkaline solutions.

The amino structure of 4-aminoquinoline is also confirmed by measurements of its dipole moment [28] ($\mu$ 4.4 D), which is considerably higher than the dipole moment of quinoline [29] ($\mu$ 2.18 D).

With the objective of detecting the two hypothetical tautomeric forms, we studied the absorption spectra of 2- and 4-aminoquinolines in a large number of organic solvents and in acid and alkaline media, both immediately and after the passage of a few days after preparation of the solutions. If a tautomeric equilibrium had been established, we should expect to find the "benzene-quinoneimine" bands (of the imino form) superposed on the "benzene-aminopyridine" bands (of the amino form), but no evidence of this could be found on careful examination. Changes took place in the absorption spectra of 2- and 4-aminoquinolines in acid solutions when the quantity of acid was more than 5-10 moles per mole of these compounds. These can be correlated with the usual reactions of salt formations at the ring nitrogen, and are not due to tautomeric transformations.

It has been noted [30] that the existence of heterocyclic amines in the amino form is caused by displacement of the amino-imino equilibrium towards the side of the amino form to the extent to which the basicity constant of the imino form exceeds the basicity constant of the amino form. A concentration of the imino form in solutions which is not detectable by the spectral method nevertheless does not exclude the possibility of a reaction involving tautomeric transformation of the amino form into the imino form. At the same time we can accept the views of A. N. Nesmeianov [31, 32] and explain the dual reactivity of 2- and 4-aminoquinolines by conjugation of groups and transfer of the reactive center from the ring nitrogen to the amino group, and conversely in dependence upon the reaction conditions and the influence of the reagent used.

## SUMMARY

1. The influence of solvents and of acid and alkaline solutions on the absorption spectra of 2- and 4-aminoquinolines, 4-acetylaminoquinoline and 1-methyl-4-iminoquinoline was studied.

2. It was established that in solvents with little effect on the ring nitrogen (hexane, dioxane), the "benzene-pyridine" spectrum predominates in the case of 2- and 4-aminoquinolines, and the "benzene-quinoneimine" spectrum in the case of 1-methyl-4-iminoquinoline.

3. It was established that under the influence of ionizing solvents and hydrochloric acid of various concentrations the "benzene-pyridine" spectrum of 2- and 4-aminoquinolines remains substantially unaltered, but "o- or p-aminopyridine" bands are developed which indicate conjugation of the positively charged ring nitrogen with the ring and with the 2- or 4-amino group.

4. It was shown that formation of the doubly-charged ions of 2- and 4-aminoquinolines in concentrated sulfuric acid is accompanied by reversion to the spectrum of the unsubstituted quinolinium ion.

5. The ultraviolet absorption spectra of 2- and 4-aminoquinolines indicate the absence of tautomerism of these compounds.

## LITERATURE CITED

[1] E. A. Steck, G. W. Ewing, J. Am. Chem. Soc. 70, 3404 (1948).

[2] J. M. Hearn, R. Morton, J. Simpson, J. Chem. Soc. 1951, 3321, 3328.

[3] S. J. Angual, R. L. Werner, J. Chem. Soc. 1952, 2911.

[4] A. E. Chichibabin and O. A. Zeide, J. Russ. Chem. Soc. 46, 1232 (1914); compare Shreve and others, Ind. Eng. Chem. 32, 177 (1940).

[5] R. C. Elderfield and others, J. Am. Chem. Soc. 68, 1250 (1946).

[6] O. Magidson, A. Grigorovski, Ber. 69, 408 (1936).

[7] Ad. Claus, W. Frobenius, J. pr. Ch. (2) 56, 184 (1897).

[8] A. Albert, B. Ritchie, J. Chem. Soc. 1943, 458.

[9] V. I. Bliznlukov and N. T. Solonskaia, Collection of Studies of Ukrainian Pharmacists, State Publishing House of Medical Literature of the Ukrainian SSR 12 (1956).*

[10] V. I. Bliznlukov, Proc. Acad. Sci. USSR 91, 1337 (1953).

[11] V. I. Bliznlukov, J. Gen. Chem. 22, 1204 (1952).**

[12] A. Albert, R. Goldacre, Nature 153, 468 (1944).

[13] S. J. Angual, C. L. Angual, J. Chem. Soc. 1952, 1461.

[14] N. L. Drake and others, J. Am. Chem. Soc. 68, 1214 (1946).

[15] J. L. Irvin, E. M. Irvin, J. Am. Chem. Soc. 69, 1091 (1947).

[16] F. Wenzel, Monatsh. 15, 457 (1894).

[17] Ad. Claus, H. Howitz, J. pr. Ch. (2) 50, 237 (1894).

[18] Ad. Claus, W. Frobanius, J. pr. Ch. (2) 56, 190 (1897).

[19] R. R. Renshaw, H. L. Fridman, F. I. Gajewski, J. Am. Chem. Soc. 61, 3322 (1939).

[20] H. Coates, A. H. Cook, I. M. Heilbron, J. Chem. Soc. 1943, 402.

[21] Ad. Claus, S. Schaller, J. pr. Ch. (2) 56, 206 (1897).

[22] W. Roser, Lieb. Ann. 282, 381 (1894).

[23] W. Marcwald, Lieb. Ann. 279, 18 (1894).

[24] A. Tschitschibabin, D. Witkovski, M. Lapschin, Ber. 58, 803 (1925).

[25] G. Morgan, I. Stewart, J. Chem. Soc. 1938, 1295.

[26] L. Marchlewski, A. Moroz, Bull. Soc. Chim. 35, 473 (1924).

[27] F. Klingstedt, C. r. 176, 1550 (1923).

[28] D. G. Lies, D. C. Curran, J. Am. Chem. Soc. 67, 79 (1945).

[29] K. S. Topchiev, M. M. Iakshin and O. E. Shindel, Proc. Acad. Sci. USSR 30, 502 (1941).

[30] Iu. N. Sheinker, V. V. Kushkin and I. Ia. Postovskii, J. Phys. Chem. 31, 224 (1957).

[31] A. N. Nesmeianov and M. I. Kabachnik, J. Gen. Chem. 25, 41 (1955).**

[32] M. I. Kabachnik, Prog. Chem. 25, 137 (1956).

[33] N. A. Valiashko and Iu. S. Rozum, J. Gen. Chem. 17, 757 (1947).

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* In Russian.

** Original Russian pagination. See C. B. Translation.

# THE ABSORPTION SPECTRA AND STRUCTURE OF ACRIDINE

V. I. Bliznlukov and A. K. Sukhomlinov

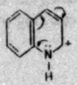
Many studies have been made [1-4] of the spectrography of acridine. We studied the absorption spectra of acridine in ethanol, dioxane, carbon tetrachloride, dichloroethane, ethanolic hydrochloric acid of various concentrations, 98% sulfuric acid, and 60% perchloric acid at concentrations of $10^{-3}$ to $10^{-5}$ molar.

The absorption spectrum of acridine has the general character of the quinoline spectrum [5], but under the influence of the condensed benzene ring it is very much displaced toward longer waves in comparison with the quinoline spectrum. Thus, the long-wave band of acridine is bathochromically displaced by about 400 A, and the short-wave band by 200-300 A (Fig. 1, curves 1, 2; compare 3; curves 4 and 5, compare 6). In addition the long-wave band is 3-5 times more intense and the short-wave bands 5-8 times more intense than the quinoline bands. Due to this heightened intensity of the bands, arbitrarily called "benzene" bands, the "pyridine" band of acridine with $\lambda_{max}$ 3100 A and $\epsilon$ 2500, is covered by the edge of the long-wave "benzene" band, and therefore in the spectrum of acridine in solution in dioxane or hexane the "pyridine" band is not sharp (Fig. 1, curves 2, 4, compare with 3 and 6). The sharper "pyridine" band of acridine with a fine structure is detected in the spectrum of 9-aminoacridine in hydrochloric acid solution (Fig. 1, curve 7).

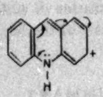
Formation of an acridine salt is accompanied by a bathochromic shift of the long-wave edge of the acridine band by 200 A and by a relatively small bathochromic shift of the edge of its short-wave band. A broad absorption band with $\lambda_{max}$ 3980 A and $\epsilon$ 3200 is formed at the start of the visible region (Fig. 2, curves 1-3). In form and position this band can be classed with the "ortho type" of benzene bands [6]. The other short-wave band of the "ortho type," with an orientatory maximum at $\lambda$ 2500-2600 A is not observed in the spectrum of the acridine salt, since presumably it falls into the region of absorption of the stronger short-wave "benzene" band of acridine which is approximately in the same region. A short-wave band of the "ortho type" is observed in the spectrum of the salt of 9-acetyl-aminoacridine (see Fig. 2, curve 5).

Judging by the nature of the absorption, the spectrum of the acridinium ion is a complex one; it consists of "benzene" bands, as in anthracene, on which are superposed "benzene" bands of the "ortho type" (Fig. 2, curves 6, 7, 8 and 10). The same bands of the "ortho type" are found in the spectrum of the quinolinium ion, but in the case of the acridinium ion they are considerably shifted toward the visible region just as in the case of the ion of 6-aminoquinoline (Fig. 2, curve 9).

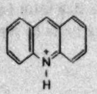
The development of "benzene" bands of the "ortho type" in the spectrum of the acridinium ion is evidently due to the ability of the positive charge in the acridinium ion to move from the ring nitrogen to the carbon atom in the 3 (6) position (formula II), just as the positive charge of the quinolinium ion can move from the ring nitrogen to the second carbon atom [5] (formula I).



(I)



(II)



(III)

The presence of the "benzene" absorption bands of the same type as in anthracene may indicate, however, that the aromatic system of the pyridine ring with a positive charge at the ring nitrogen is retained intact in the acridinium ion (formula III).

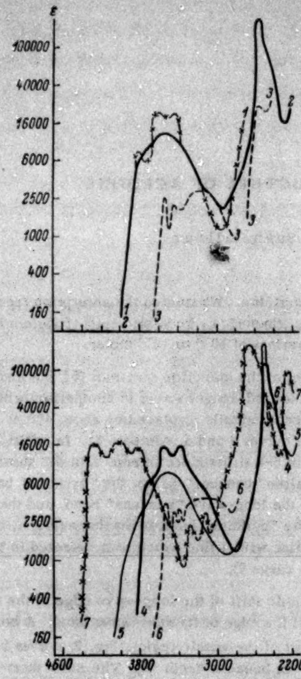


Fig. 1. Absorption spectra. 1) Acridine in $CCl_4$; 2) acridine in dioxane; 3) quinoline in ethanol [5] (the long-wave branch of the curve is bathochromically displaced by 400 A, and the short-wave band is displaced by 300 A); 4) acridine in hexane; 5) acridine in ethanol; 6) quinoline in hexane [5] (the long-wave branch of the curve is bathochromically displaced by 400 A, and the short-wave branch by 200 A); 7) 9-aminoacridine in standard HCl solution (molar ratio 1:1).

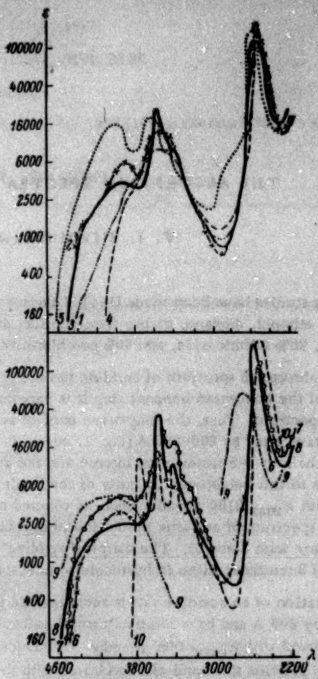


Fig. 2. Absorption spectra. 1) Acridine in standard HCl solution (molar ratio 1:0.2); 2) acridine in standard HCl solution (molar ratio 1:1); 3) acridine in standard HCl solution (molar ratio 1:100); 4) acridine in ethanol; 5) 9-acetyl-9-aminoacridine in 60% $HClO_4$; 6) acridine in 5 M ethanolic HCl; 7) acridine in 60% $HClO_4$; 8) acridine in concentrated $H_2SO_4$; 9) 6-aminoquinolinium ion (part of curve); 10) anthracene in hexane.

These data from the spectrographic investigation, which demonstrate the weakening of the aromatic character of the pyridine ring of acridine after salt formation, are in harmony with oxidation data. Thus, the acridinium ion is oxidized at the pyridine ring with formation of acridone [7]. On the other hand, the oxidation of acridine in an alkaline medium easily leads to rupture of the benzene ring with formation of quinoline-2,3-dicarboxylic acid [8].

## SUMMARY

1. Acridine in organic solvents gives a complex ultraviolet absorption spectrum containing bands characteristic of the pyridine (quinoline) ring and benzene. The reciprocal influence of the rings is reflected in a

heightening of intensity and in a shift of the respective absorption bands toward the long-wave region.

2. The absorption spectrum of the acridinium ion in acid solutions is regarded as a complex spectrum comprising the benzene bands of "anthracene" and benzene bands of the "ortho type" which are superposed.

## LITERATURE CITED

[1] Radulescu, Ostrogovitch, Ber. 64, 2233 (1931).

[2] G. A. Dima, P. Pogangeanu, Bull. Sect. Sci. Acad. Roumanie, 21, 38 (1938).

[3] D. P. Craig, L. H. Short, J. Chem. Soc. 1945, 419.

[4] B. Charlampowiczowna, M. Marchlewski, Bull. Acad. Polonaise, A 1930, 376.

[5] V. I. Blizniukov and N. T. Solonskaia, Symposium on "Some Problems of Pharmacy," State Publishing House of Medical Literature of the Ukrainian SSR 12 (1956);* compare: V. I. Blizniukov, Proc. Acad. Sci. USSR 91, 1337 (1953).

[6] V. I. Blizniukov and V. M. Reznikov, J. Gen. Chem. 25, 402 (1955).**

[7] C. Graebe, K. Lagodzinski, Lieb. Ann. 276, 35 (1893).

[8] C. Graebe, H. Caro, Ber. 13, 99 (1880).

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* In Russian.

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# RELATION BETWEEN THE ACIDITY OF ACYCLIC POLYOLS AND THE LENGTH OF THE POLYHYDROXYMETHYLENE CHAIN

## L. A. Mai

The acidity of acyclic polyols (polyhydric alcohols) depends in great measure on the length of the polyhydroxymethylene chain [1]. We established that the relation between the dissociation constants (K) of polyols of the structure $HOCH_2(CHOH)_nCH_2OH$ and the number of CHOH groups (n) can be expressed by the following formula when n is 0, 1, 2 or 4:

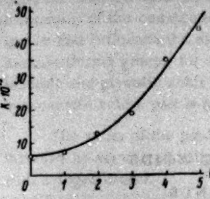
$$K(n) = a + bn^c,$$
$$\text{where } a = 6\cdot 10^{-15},\ b = 1\cdot 10^{-15},\ c = 2.3. \qquad (1)$$

In order to check this interesting functional dependence we determined the acidity constants of xylitol (n = 3) and D-gluco-D-guloheptitol (n = 5) by an approximate electrometric method. The values are in good agreement with those calculated from equation (1) (see table).

| *n* | Compound | *pK* found from expt. | *pK* from equation (1) |
|---|---|---|---|
| 0 | Ethylene glycol | 14.24 [1] | 14.22 |
| 1 | Glycerine | 14.16 [1] | 14.16 |
| 2 | Meso-erythritol | 13.90 [1] | 13.96 |
| 3 | Xylitol | 13.73 | 13.73 |
| 4 | Dulcitol | 13.46 [1] | 13.52 |
| 5 | D-gluco-D-guloheptitol | 13.35 | 13.33 |

We also determined the acidity constant of D-mannitol in order to confirm the absence of error that could have crept in on comparison of the values of Michaelis (1913) [1] for the acidity constants of polyols with n = 0, 1, 2 and 4 with our own data for polyols with n = 3 and 5. The difference between our value ($K = 3.80 \times 10^{-14}$, pK = 13.42) and the value found by Michaelis ($K = 3.4 \times 10^{-14}$, pK = 13.47) lies within the limits of error of measurement. An error of between ±0.05 and 0.1 pH must be assumed in measurements of pH in the vicinity of 14 with the hydrogen electrode, due to the indeterminate character of the diffusion potential, the low degree of buffering of the solutions, and other factors.

The acidity of the acyclic polyols therefore appreciably increases with the length of the polyhydroxymethylene chain, at least up to the hexitols-heptitols. Due to the absence of data for octitols and nonitols it is impossible at present to predict the character of the further change of acidity with chain length; it is highly probable that with increasing number of CHOH groups between the $CH_2OH$ groups beyond 5, the acidity will gradually approach an asymptotic value (see diagram).



Acidity constant K of polyols $HOCH_2(CHOH)_nCH_2OH$ as a function of the number of CHOH groups (n).

## EXPERIMENTAL

Xylitol was prepared from D-xylose by reduction with sodium amalgam [2]: a colorless, non-crystallizing syrup; m. p. of the dibenzal derivative 172-174°. D-Gluco-D-guloheptitol was prepared from D-gluco-D-guloheptonolactone by reduction with sodium amalgam [3] and was recrystallized from methanol; m. p. 126-127°.

$CO_2$-free double-distilled water and $CO_2$-free alkali were used in the measurements which were performed with a hydrogen electrode at 18°. The measuring cell comprised $Pt-PtO_2-H_2$ | solution of polyol and its salt | saturated KCl solution | saturated calomel electrode. The ionic strength of the solutions was 0.01; the concentration of the polyol was 0.5 M and that of the NaOH 0.01 M. The mean of three independent measurements was taken. The error of measurement was ± 0.05-0.1 pH.

## SUMMARY

1. The acidity constants of xylitol, D-mannitol and D-gluco-D-guloheptitol were determined by an approximate electrometric method.

2. The acidity of the acyclic polyols increases with the chain length, at least as far as the hexitols-heptitols.

3. A functional relation between dissociation constants of acyclic polyols and chain length was found, in good agreement with the experimental data.

## LITERATURE CITED

[1] L. Michaelis, Ber. 46, 3683 (1913).

[2] E. Fischer, Ber. 27, 2487 (1894).

[3] E. Fischer, Lieb. Ann. 270, 80 (1892).

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# THE ACIDITY OF SOME MONOSUBSTITUTED ACETIC ACIDS AND THE ELECTRONIC AFFINITY OF SUBSTITUENTS

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The increased acidity of polar-substituted acetic acids in comparison with acetic acid itself is known to be due to the electrostatic effect of the substituting atom or atomic group. The functional relation between the magnitude of the acidity constant of monosubstituted acetic acids and the nature of the substituent is of interest for the study of the reciprocal influence of atoms in such molecules.

It has been suggested that the change in acidity of monohalosubstituted acetic acids ($\Delta pK$) due to a polar substituent is exclusively a field effect:

$$\frac{\Delta pK}{E} = \text{const},$$

where E is the dipole field [1]. However, the most recent values of pK of monohalosubstituted acetic acids, obtained by very accurate conductometric measurements [2], do not reveal very good constancy of the $\Delta pK/E$ ratio; in addition to the field effect (if this is involved) an other electrostatic factor must evidently come into play: the polarizability of the halogen–carbon bond [2].

Dissociation Constants of Some Monosubstituted Acetic Acids and the Electronic Density of the Substituents

| Substituent | −log K | E (ev) [3] | −E log K |
|---|---|---|---|
| F | 2.59 | 4.03 | 10.44 |
| Cl | 2.87 | 3.74 | 10.73 |
| Br | 2.90 | 3.65 | 10.58 |
| I | 3.17 | 3.30 | 10.46 |
| CN | 2.47 | 3.60 | 8.89 |
| OH | 3.83 | 2.16 | 8.27 |
| SH | 3.54 | 2.60 | 9.20 |

We established that for monohalosubstituted acetic acids as well as for cyanoacetic, mercaptoacetic and glycolic acids there is a reciprocal proportionality between the energy of acid dissociation (energy expended on removal of a proton from the COOH group) and the electronic affinity of the substituent (energy expended on removal of an electron from the corresponding anion); the energy of the reaction

$$XCH_2COO^- + H^+ \rightarrow XCH_2COOH$$

is inversely proportional to the energy of capture of an electron by the substituting atom or group $X + e^- \rightarrow X^-$, i.e., $-E\log K = \text{const.}$ or $K^E = \text{const.}$, where E is the electronic affinity of the given atom or atomic group. For halogens $-E\log K = 10.55$ ev, and $K^E = 2.818 \times 10^{-11}$; for OH-, SH- and CN-substituted acetic acids, these constants are respectively 8.79 ev, and $1.622 \times 10^{-9}$. For halo-substituted acetic acids the deviation of the value of $-E\log K$ from the mean does not exceed ± 0.18. The value of $-E\log K$ varies rather more in the cases of

OH-, SH- and CN-substituted acetic acids (see table); the deviations of 0.52 are evidently due not only to the inaccuracy of the corresponding values of the dissociation constants and electronic affinity but mainly to other factors that influence the dissociation of these acids and that are associated with the more complex structure of the substituting groups; for example the presence of a second ionizable H atom at the O and S atoms in mercaptoacetic and glycolic acids and the possibility of formation of a cyclic structure through a hydrogen bond. In cyanoacetic acid a part is played by the dipole $\bar{N}\equiv\overset{+}{C}$.*

The value of the product −Elog K for acetic acid (3.38) is very different from the constants listed above; this may be associated with the unique electronic structure of the hydrogen atom which prevents comparison with halogen atoms.

The relatively good constancy of −Elog K for monohalosubstituted and also (as we must assume) for other monosubstituted acetic acids may provide an opportunity for determining (or at least for evaluating) the electron affinity of some atoms and atomic groups such as astatine (halogen 85), SeH, TeH, SCN, $\overset{+}{N}H_3$, etc., independently of methods known at the present time (energy of the crystalline, ionic lattice with the help of the Haber-Born cycle, the space charge, the absorption spectra, the minimum electron-acceleration voltages for ionization of gases, or extrapolation from the isoelectronic series).

The relation in question of course does not allow conclusions to be reached about the mechanism of the reciprocal influence of a substituent and the protonizable H atom of the COOH group. In the case of halogen substituents, however, the most probable mechanism is a shift of electronic density from atom to atom along a chain of covalent bonds; this mechanism is supported by the marked inverse proportionality of the energy of dissociation and the electron affinity of a halogen which characterizes the tendency to complete the octet.

## SUMMARY

The dissociation constants of monohalosubstituted acetic acids are inversely proportional to the magnitudes of the electronic affinities of the halogen. The same relation also applies to cyanoacetic, glycolic and thioglycolic acids, but the latter have a different value of the constant −Elog K.

## LITERATURE CITED

[1] D. J. G. Ives, K. Sames, J. Chem. Soc. 1943, 513, Ch. A. 38, $1163^{8,9}$ (1944).

[2] D. J. G. Ives, J. H. Pryor, J. Chem. Soc. 1955, 2104.

[3] Short Handbook of Physicochemical Constants [In Russian] (State Chemical Press, Leningrad 1955), p. 66.

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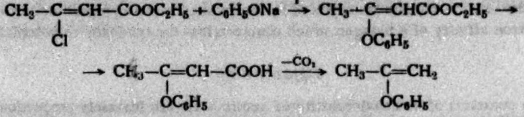
* It is interesting to note that the dissociation constants of cyanoacetic acid (2.47) and glycine for $H_3\overset{+}{N}CH_2COOH \rightleftharpoons H^+ + H_2NCH_2COOH$(2.40) are very similar.

# SYNTHESIS AND TRANSFORMATIONS OF SUBSTITUTED VINYL ETHERS

## VI. SYNTHESIS OF α-METHYLVINYL ARYL AND α-METHYLVINYL CYCLOHEXYL ETHERS

M. F. Shostakovskii, E. P. Gracheva and N. K. Kul'bovskaia

α-Methylvinyl aryl ethers have not been extensively studied. Two methods for their preparation have been described. Ruhemann and Wragg [1] synthesized α-methylvinyl phenyl ether by the reactions

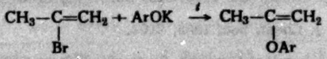


$$CH_3-\underset{\substack{|\\Cl}}{C}=CH-COOC_2H_5 + C_6H_5ONa \xrightarrow{t} CH_3-\underset{\substack{|\\OC_6H_5}}{C}=CHCOOC_2H_5 \rightarrow$$

$$\rightarrow CH_3-\underset{\substack{|\\OC_6H_5}}{C}=CH-COOH \xrightarrow{-CO_2} CH_3-\underset{\substack{|\\OC_6H_5}}{C}=CH_2$$

The efficiency of the method is not, however, stated in the paper.

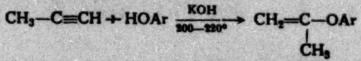
Niederl and Storch [2] isolated the phenyl and cresyl ethers by the action of isopropenyl bromide on the corresponding potassium phenoxide.



$$CH_3-\underset{\substack{|\\Br}}{C}=CH_2 + ArOK \xrightarrow{t} CH_3-\underset{\substack{|\\OAr}}{C}=CH_2$$

This reaction is limited mainly by the poor availability of isopropenyl bromide and by the low yield of the ether.

In the present work we studied the conditions of synthesis of α-methylvinyl aryl and α-methylvinyl cyclohexyl ethers by the method of Favorskii and Shostakovskii.



$$CH_3-C\equiv CH + HOAr \xrightarrow[200-220^\circ]{KOH} CH_2=\underset{\substack{|\\CH_3}}{C}-OAr$$

The employment of propyne as the vinylating agent leads to a lower yield in comparison with the vinylation of phenols with acetylene [3, 4]. This method is nevertheless more convenient than any of the existing methods of preparation of α-methylvinyl aryl ethers. A study of the conditions for this synthesis established that partial prevention of resinification and improvement of the yields of α-ethers necessitates the use of 1 mole of potassium hydroxide per mole of phenol and an excess of propyne (Table 1).

In all cases, however, a considerable amount of resin is obtained; its nature will be investigated later.

We undertook a study of the effect of propadiene in this reaction. Propadiene is present in the original mixture [5] and is formed by isomerization

$$CH_3C\equiv CH \rightleftarrows CH_2=C=CH_2$$

TABLE 1

| Substance vinylated (1 mole) | Quantity of KOH in the form of 66% aqueous solution (moles) | Quantity of propyne (moles) | Reaction temperature | Duration of experiment (hours) | % yield |
|---|---|---|---|---|---|
| Phenol | 1 | 2 | 220° | 4 | 40 |
| Phenol | 0.3 | 2 | 220 | 9 | 5 |
| Phenol | 1 | 2 | 220 | 2 | 10 |
| Phenol | 1 | 1 | 220 | 4 | 4 |
| Guaiacol | 1 | 2 | 200 | 10 | 35 |
| Guaiacol | 0.5 | 2 | 200 | 10 | 7 |
| m-Cresol | 1 | 2 | 220 | 6 | 31 |
| m-Cresol | 0.3 | 2 | 220 | 6 | 4 |
| Cyclohexanol* | 1 | 2 | 220 | 3 | 58 |
| Cyclohexanol | 0.5 | 2 | 220 | 3 | 36 |

TABLE 2

| Substance vinylated (1 mole) | Vinylating agent (2 moles) | Reaction temperature | Duration of experiment (hours) | % Yield |
|---|---|---|---|---|
| Phenol | Propyne | 220° | 8 | 40 |
| Phenol | Propadiene | 220 | 8 | 20 |
| Guaiacol | Propyne | 200 | 10 | 35 |
| Guaiacol | Propadiene | 200 | 10 | 17 |

We knew from the work of A. E. Favorskii [6] that the isomerization of acetylenic to allenic hydrocarbons is a reversible reaction. In the case of propadiene and propyne the equilibrium is shifted in the direction of propyne. Physicochemical calculations show [7] that the equilibrium mixture contains about 10% of propadiene and 90% of propyne at 200°. Propadiene readily isomerizes to propyne over various catalysts at elevated temperatures [8, 9]. In order to ascertain the behavior of propadiene under our conditions, we heated propadiene in an autoclave at 200° with 50% potassium hydroxide solution. It was found that propadiene isomerizes to propyne under these conditions, and the propyne was isolated as the acetylide. Propadiene did not polymerize [10] under these conditions. A comparison of the experiments on vinylation of phenols with propadiene and propyne (Tables 1 and 2) leads to the conclusion that propadiene is not the vinylating agent but isomerizes to propyne which then enters into the vinylation reaction [11].

The structure of the synthesized $\alpha$-methyl-substituted ethers was confirmed by hydrolysis. $\alpha$-Methylvinyl aryl ethers, like vinyl aryl ethers [9], are hydrolyzed under considerably more drastic conditions than $\alpha$-methylvinyl alkyl ethers [12, 13].

## EXPERIMENTAL

Propyne was prepared by the method of Hurd et al [5]. A weighed quantity of propyne was run into an autoclave which had previously been cooled with dry ice; propadiene [5, 14] was charged into an autoclave under similar conditions; the phenol had b. p. 181-182°, guiacaol b. p. 72° (6 mm), m-cresol b. p. 90° (12 mm), cyclohexanol b. p. 160.5°; the potassium hydroxide was the chem. pure grade.

1. Preparation of $\alpha$-methylvinyl phenyl ether. Into a 1-liter Bergius rotating autoclave, fitted with electrical heater, thermocouple and acetylene manometer, were charged 135 g of phenol, 81 g of potassium hydroxide dissolved in 40 ml of water, and 115 g of propyne. The autoclave was heated for 4 hours at 220°. Maximum pressure 70 atm, residual pressure 20 atm. The autoclave was cooled, the propyne was collected in a trap immersed

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* Cyclohexanol was vinylated without water.

in Dewar flask containing dry ice. 10 g of propyne was collected. The discharged product was a light-brown liquid which was distilled in vacuo. 1st fraction, b.p. 60-64° (12 mm), 82 g; 2nd fraction, 81-90° (12 mm), 5 g. The residue was 40 g of resin. The 1st fraction was dried with calcium chloride and distilled to give 80 g of α-methylvinyl phenyl ether (40%).

B. p. 61-62° (16 mm), 168-169° (756 mm), $d^{20}_4$ 0.9551, $n^{20}$D 1.5050, $MR_D$ 41.68; calculated 41.34.

Found %: C 80.53, 80.49; H 7.51, 7.58. $C_9H_{10}O$. Calculated %: C 80.60; H 7.52.

Literature data: b. p. 169°, $d^{23}_4$ 0.998, $n^{22}$D 1.5172 [1, 2].

TABLE 3

| Ether being hydrolyzed | Amount of ether determined (in %) |
|---|---|
| α-Methylvinyl phenyl | 97.4, 96.0 |
| α-Methylvinyl m-cresyl | 97.2, 97.3 |
| α-Methylvinyl guaiacyl | 94.3, 92.7 |
| α-Methylvinyl cyclohexyl | 93.2, 94.0 |

2. Preparation of α-methylvinyl guiacyl ether. The reaction was performed in a 250-ml autoclave by the above procedure, starting from 62 g of guiacol, 28 g of potassium hydroxide dissolved in 14 ml of water, and 40 g of propyne. The autoclave was heated for 10 hours at 200°. Maximum pressure 84 atm, residual pressure 40 atm. 10 g of propyne was collected. The discharged product was fractionated with steam. The distillate was dried over calcium chloride and fractionally distilled in vacuo at 99-103° (18 mm). Elimination of guaiacol from the product was effected by dissolution in absolute ether and redistillation in vacuo. 26.3 g of α-methylvinyl guiacyl ether (32%) was obtained.

B. p. 71-72° (3 mm), 202-203° (742 mm), $d^{20}_4$ 1.0392, $n^{20}$D 1.5205, $MR_D$ 47.98; calculated 47.60.

Found %: C 72.75, 72.72; H 7.22, 7.28. $C_{10}H_{12}O_2$. Calculated %: C 73.14; H 7.36.

3. Preparation of α-methylvinyl m-cresyl ether. 40 g of propyne, 54 g of m-cresol and 28.5 g of potassium hydroxide in 14 ml of water were charged into a 250-ml autoclave by the previous procedure. The mass was heated for 6 hours at 220°, and 117 g of a light-yellow, two-layered liquid was discharged. The upper layer was washed and dried and distilled to give 25 g of α-methylvinyl m-cresyl ether with b. p. 76.5-79° (14 mm). 38 g of resin remained in the flask. The viscous lower layer was steam-distilled to give 7 g of the ether. Both of the portions of ether were dried over calcium chloride. Total yield 27 g of α-methylvinyl m-cresyl ether (31%).

B. p. 78-79° (14 mm), $d^{20}_4$ 0.9444, $n^{20}$D 1.5051, $MR_D$ 46.55; calculated 45.95.

Found %: C 81.04, 80.79; H 8.11, 8.14. $C_{10}H_{12}O$. Calculated %: C 81.16; H 8.14.

Literature data: b. p. 188-189°, $d^{21}_4$ 0.978, $n^{21}$D 1.5117 [2].

4. Preparation of α-methylvinyl cyclohexyl ether. 40 g of propyne, 50.7 g of cyclohexanol and 28.5 g of potassium hydroxide were charged into an autoclave by the above procedure. The autoclave was heated for 4 hours at 220°; 70 g of light-yellow liquid was discharged. It was distilled in vacuo. 1st fraction 52-53° (12 mm), 46 g; 2nd fraction 53-140° (12 mm), 7 g. Residue: 7 g of resin. Redistillation of the 1st fraction gave 44 g of α-methylvinyl cyclohexyl ether:

B. p. 52-53° (12 mm), 162-163° (752 mm), $d^{20}_4$ 0.9176, $n^{20}$D 1.4551, $MR_D$ 41.48; calculated 42.74.

Found %: C 77.14, 76.94; H 11.61, 11.41. $C_9H_{16}O$. Calculated %: C 77.09; H 11.50.

5. Isomerization of propadiene to propyne in 50% potassium hydroxide solution. 21 g of propadiene, 7 g of potassium hydroxide in 7 ml of water were charged into a 250-ml autoclave. The mass was heated for 6 hours at 200°. Pressure 49 atm; 20 g of gas was discharged. Repeated passage through Ilosvay solution led to separation of a voluminous light-yellow precipitate of acetylide. The residue was 3 g of propadiene.

6. Hydrolysis of α-methylvinyl aryl and α-methylvinyl cyclohexyl ethers was effected with a solution of hydroxylamine hydrochloride at pH 2.9 [15]. Samples of ether weighing 0.2-0.3 g and 25 ml of hydroxylamine hydrochloride solution were charged into 40-ml ampoules which were then sealed, immersed in a boiling water bath and shaken for 4 hours at intervals of 15 minutes. The ampoules were then cooled and the contents transferred to a beaker. The acetone content was estimated from the amount of hydrochloric acid released. The

liquid was potentiometrically titrated with 0.1 N NaOH solution (methyl orange indicator) to pH 4. Results of the hydrolysis are presented in Table 3. The following formula was applied:

$$\% \text{ hydrolysis} = (a \cdot M \cdot 1.057 \cdot 100) / w \cdot 10000$$

where $\underline{a}$ is the number of milliliters of 0.1 N sodium hydroxide solution consumed in titration of the acid released during the reaction (difference between the actual and a blank experiment); M is the molecular weight of the ether, 1.057 is a factor to allow for the reaction between acetone and hydroxylamine proceeding to the extent of 94.4% [16], and $\underline{w}$ is the weight of ether.

## SUMMARY

1. A procedure was developed for the preparation of α-methylvinyl aryl and α-methylvinyl cyclohexyl ethers by the Favorskii-Shostakovskii method. α-Methylvinyl guaiacyl and α-methylvinyl cyclohexyl ethers were prepared for the first time.

2. It was shown that propadiene isomerizes in an alkaline medium to propyne, the latter being the vinylating agent.

3. The prepared ethers were hydrolyzed by a specially developed procedure.

## LITERATURE CITED

[1] S. Ruhemann, F. Wragg, J. Chem. Soc. 79, 1190 (1901).

[2] J. B. Niederl, E. A. Storch, J. Am. Chem. Soc. 55, 291 (1933).

[3] M. F. Shostakovskii and M. S. Burmistrova, J. Appl. Chem. 15, 260 (1942).

[4] M. F. Shostakovskii, V. P. Shishkov and M. G. Zelenskaia, J. Appl. Chem. 24, 1166 (1951).*

[5] C. D. Hurd, R. N. Meinert, L. U. Spence, J. Am. Chem. Soc. 52, 1141 (1930).

[6] A. E. Favorskii and K. L. Debu, J. Russ. Chem. Soc. 29, 78 (1896).

[7] D. A. Frank-Kamenetskii and V. G. Markovich, J. Gen. Chem. 12, 619 (1942).

[8] L. M. Slobodin, J. Gen. Chem. 6, 1892 (1936).

[9] United States Patent 2594706 (1952); Chem. Abs. 47, 1180 (1953).

[10] S. V. Lebedev, J. Russ. Chem. Soc. 45, 1357 (1913).

[11] A. E. Favorskii, J. Russ. Chem. Soc. 24, 291 (1913).

[12] M. F. Shostakovskii and E. P. Gracheva, J. Gen. Chem. 23, 1153 (1953).*

[13] M. F. Shostakovskii and E. P. Gracheva, J. Gen. Chem. 23, 1320 (1953).*

[14] G. G. Gustavson, J. Russ. Chem. Soc. 20, 615 (1888).

[15] M. F. Shostakovskii, Vinyl Ethers [in Russian] (1952), p. 261-264.

[16] M. Marasco, Ind. Eng. Ch. 18, 701 (1926).

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Academy of Sciences of the USSR

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* Original Russian pagination. See C. B. Translation.

# INTERACTION OF HALIDES OF TRIVALENT IRON WITH NICOTINE

S. F. Babak and G. B. Kagramanova

Reaction of nicotine with halides of zinc [1], mercury [2] and copper [3] in a medium of the corresponding hydrogen halides gave compounds whose composition and properties identify them as salts of nicotine and of free halogen acids with the general formula $HM\Gamma_3$ or $H_2M\Gamma_4$, where M is metal and $\Gamma$ is chlorine, bromine or iodine.

In the present work we describe for the first time the results of a study of the reaction of nicotine with halides of trivalent iron both in presence of the corresponding hydrogen halides and in neutral, aqueous and alcoholic media.

## EXPERIMENTAL

Nicotine was prepared and purified as previously described [4]. The ferric chloride was the chem. pure grade. Ferric bromide was prepared as described by Kariakin [5]; the iodide was prepared in similar fashion. Hydrochloric acid was purified by distillation; hydrobromic and hydriodic acids were prepared and purified as described in [5]. Ethyl alcohol (commercial) was twice distilled.

$FeCl_3 \cdot C_{10}H_{14}N_2 \cdot 2HCl$ was prepared by dissolving 2.75 g of ferric chloride in 20 ml of concentrated hydrochloric acid and adding 1.62 g of nicotine dropwise with vigorous stirring. The transparent brownish-yellow solution was put into a crystallizer and deposited yellow crystals after a few days at room temperature. Yield of uncrystallized product 67%. The substance was recrystallized from water and dried to constant weight at 100-105°. The salt had m. p. 188-189° (with decomp.); its solubility in water at 25° was 46.01%. It dissolved readily in methyl and ethyl alcohols; it was poorly soluble in acetone and insoluble in benzene and ether; the pH (determined potentiometrically) of this salt on dilution of 1 mole to 1000 liters was 2.74. The molecular electrical conductivity of the same solution at 25° was $1070\Omega^{-1}cm^2$. The halogen content was determined by the Volhard method, iron by the method given in [6]; nicotine was determined by titration with sulfuric acid in presence of methyl red after it had been distilled off from the alkali solution with steam.

Found %: Fe 14.09, 14.10; Cl 44.62, 44.73; $C_{10}H_{14}N_2$ 40.77, 40.69. $FeCl_3 \cdot C_{10}H_{14}N_2 \cdot 2HCl$. Calculated %: Fe 14.21; Cl 44.63; $C_{10}H_{14}N_2$ 40.79.

A compound of the same composition is obtained in a neutral aqueous or alcoholic medium. Its properties, however, are different. It is in the form of stout, transparent, brownish-yellow crystals, m. p. 156-157°; solubility in water at 18° 4.43%; the pH of this solution is 4.48. This solution turns cloudy at above 18°, and on boiling it deposits a brown solid. The pH of the solution on dilution of 1 mole to 1000 liters is 2.84. The molecular electrical conductivity of the same solution at 25° is $1030\Omega^{-1}cm^2$.

$FeBr_3 \cdot C_{10}H_{14}N_2 \cdot 2HBr$ was prepared by dissolving 2.95 g of ferric bromide in 20 ml of concentrated hydrobromic acid and adding 1.62 g of nicotine (dissolved in 3 ml of water) dropwise with stirring. The solution was placed in a crystallizer and deposited black crystals after a few days at room temperature. They were recrystallized from water. M. p. 182-183°.

Found %: Fe 8.95, 9.18; Br 64.23, 64.57; $C_{10}H_{14}N_2$ 26.49, 26.21. $FeBr_3 \cdot C_{10}H_{14}N_2 \cdot 2HBr$. Calculated %: Fe 9.01; Br 64.50; $C_{10}H_{14}N_2$ 26.15.

Solubility in water at 25° 50.62%. Good solubility in methyl and ethyl alcohols; insoluble in diethyl ether and benzene; poorly soluble in acetone. Molecular electrical conductivity after dilution of 1 mole to 1000 liters at 25°, $1037 \Omega^{-1} cm_2$; pH 2.72.

$FeI_3 \cdot C_{10}H_{14}N_2 \cdot 2HI$ was prepared from 4.33 g of ferric iodide in 20 ml of concentrated hydriodic acid to which 1.62 g of nicotine was added. After a few days the solution deposited stout, black crystals. The salt is insoluble in water, benzene and diethyl ether; it is soluble in methyl and ethyl alcohols and acetone. Yield about 74%. M. p. 86-87°.

Found %: I 74.77, 73.98; $C_{10}H_{14}N_2$ 18.17, 19.04. $FeI_3 \cdot C_{10}H_{14}N_2 \cdot 2HI$. Calculated %: I 74.76; $C_{10}H_{14}N_2$ 18.97.

$FeI_3 \cdot C_{10}H_{14}N_2 \cdot HI$ was prepared from 4.33 g of ferric iodide dissolved in an equimolar quantity of hydriodic acid to which 1.62 g of nicotine was then added with stirring. Nearly black crystals came down after a few days and were washed with ether. Yield about 60%. Solubility in water at 25° 1.01%. Good solubility in methyl and ethyl alcohols; insoluble in benzene and ether. M. p. 98° (decomposes at 240°).

Found %: I 68.93, 68.17, 69.23; $C_{10}H_{14}N_2$ 21.72, 21.61. $FeI_3 \cdot C_{10}H_{14}N_2 \cdot HI$. Calculated %: I 69.86; $C_{10}H_{14}N_2$ 22.31; Fe 7.68.

It should be noted that the compound obtained from acid aqueous solution has a higher melting point (about 30° higher) and a much higher solubility than the compound obtained from water and alcohol. The crystals differ in color; the pH and molecular electrical conductivity of the aqueous solutions of these compounds are approximately identical. This phenomenon is evidently associated with the internal structure of these compounds and calls for closer investigation.

The melting point of solids obtained from acid solutions and which contain 2 moles of acid falls in passing from chlorides to iodides. The iodide with 1 mole of acid melts higher than that with 2 moles of acid. The halides are completely precipitated from the aqueous solutions of these salts by silver nitrate. The molecular electrical conductivity and pH of solutions of the chlorides and bromides indicate that free hydrogen, iron and halogen ions are present in solution. It therefore follows that the compounds prepared by us are salts of the corresponding chloro-, bromo- and iodoacids of iron which are completely dissociated into ions.

## SUMMARY

1. The following complex salts of nicotine with ferric chloride, bromide and iodide and the corresponding hydrogen halides were prepared: $FeCl_3 \cdot C_{10}H_{14}N_2 \cdot 2HCl$; $FeBr_3 \cdot C_{10}H_{14}N_2 \cdot 2HBr$; $FeI_3 \cdot C_{10}H_{14}N_2 \cdot 2HI$; $FeI_3 \cdot C_{10}H_{14}N_2 \cdot HI$.

2. Compounds of nicotine with haloacids of iron of the type of $C_{10}H_{14}N_2 \cdot H_2M\Gamma_5$ are completely dissociated into ions.

## LITERATURE CITED

[1] S. F. Babak and L. A. Kondrashov, J. Gen. Chem. 24, 1759 (1954).*

[2] S. F. Babak and L. A. Kondrashov, Communications of the D. I. Mendeleev All-Union Chemical Society 3, 18 (1953).

[3] S. F. Babak and G. B. Kagramanova, J. Gen. Chem. 24, 1690 (1954).*

[4] S. F. Babak, J. Gen. Chem. 19, 1604 (1949).*

[5] Iu. V. Kariakin, Pure Chemical Reagents [in Russian] (1947).

[6] E. V. Alekseevskii, R. K. Gol'ts and A. P. Musakin, Quantitative Analysis [in Russian] (1958), p. 225.

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and Samarkand Institute of Soviet Trade

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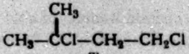
* Original Russian pagination. See C. B. Translation.

# INVESTIGATIONS ON AMINES AND QUATERNARY AMMONIUM COMPOUNDS

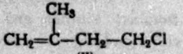
## X. PREPARATION OF ISOPRENE FROM α,β- AND γ,γ-DIMETHYLALLYL CHLORIDES

A. T. Babaian, G. M. Mkrian and R. S. Giuli-Kevkhian

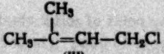
Isoprene was first synthesized by Euler [1] by exhaustive methylation of β-methylpyrrolidine. Application of the Hofmann thermal cleavage of quaternary ammonium compounds is encountered in the patent literature on isoprene synthesis [2]. Ostromyslenskii claims [3] that dichloroisopentane (I), as well as the chloroisoamylenes (II and III) lose two molecules of hydrogen chloride to give isoprene when heated with amines possessing relatively low basicity, such as p-chloroaniline and quinoline.


$CH_3-\overset{CH_3}{\overset{|}{C}}Cl-CH_2-CH_2Cl$

(I)


$CH_2=\overset{CH_3}{\overset{|}{C}}-CH_2-CH_2Cl$

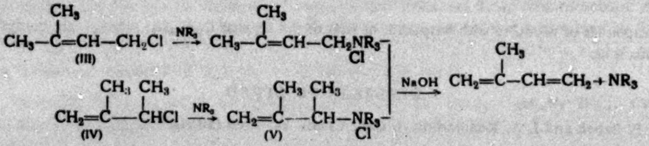
(II)


$CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CH_2Cl$

(III)

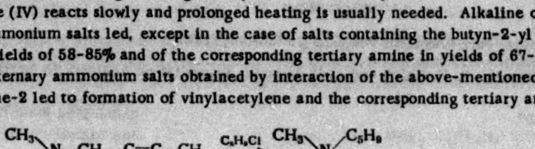
The above literature data and the results of investigations of dehydrochlorination and cleavage of quaternary ammonium salts with aqueous alkali, published in the preceding communications [4], indicated the possibility of development of a convenient method of preparation of isoprene from dichloroisopentanes and monochloroisoamylenes.

The present communication concerns the preparation of isoprene by alkaline cleavage of quaternary ammonium salts obtained by reaction of α,β- and γ,γ-dimethylallyl chlorides with tertiary amines.


$$\left.\begin{matrix} \underset{(III)}{CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CH_2Cl} \xrightarrow{NR_3} CH_3-\overset{CH_3}{\overset{|}{C}}=CH-CH_2\underset{Cl}{NR_3^-} \\ \underset{(IV)}{CH_2=\overset{CH_3}{\overset{|}{C}}-\overset{CH_3}{\overset{|}{C}}HCl} \xrightarrow{NR_3} \underset{(V)}{CH_2=\overset{CH_3}{\overset{|}{C}}-\overset{CH_3}{\overset{|}{C}}H-\underset{Cl}{NR_3^-}} \end{matrix}\right| \xrightarrow{NaOH} CH_2=\overset{CH_3}{\overset{|}{C}}-CH=CH_2+NR_3$$

Tertiary amines used in the work were dimethylisoamyl-, dimethyl(γ,γ-dimethylallyl)-, dimethylbenzyl- and dimethyl-(butyn-2-yl)-amines.

Reaction of (III) with amines goes energetically with heat development, and in some cases cooling is necessary. The chloride (IV) reacts slowly and prolonged heating is usually needed. Alkaline cleavage of the prepared quaternary ammonium salts led, except in the case of salts containing the butyn-2-yl radical, to formation of isoprene in yields of 58-85% and of the corresponding tertiary amine in yields of 67-89%. Alkaline cleavage of the quaternary ammonium salts obtained by interaction of the above-mentioned chlorides with 1-dimethylaminobutyne-2 led to formation of vinylacetylene and the corresponding tertiary amine.

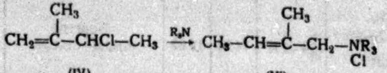

$$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>N-CH_2-C\equiv C-CH_3 \xrightarrow{C_5H_9Cl} \begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\underset{Cl}{\underset{|}{N}}\!\!<\begin{matrix}C_5H_9\\CH_2-C\equiv C-CH_3\end{matrix} \xrightarrow{NaOH}$$

$$\rightarrow CH_2=CH-C\equiv CH+\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>N-C_5H_9$$

These results testify to the lability of the butyn-2-yl radical and are consistent with our earlier results [4a, 5] on the cleavage of quaternary ammonium salts containing the butyn-2-yl radical.

Dimethyl-γ,γ-dimethylallylamine is also formed by alkaline cleavage of the quaternary ammonium salt obtained by interaction of γ,γ-dimethylallyl chloride with an aqueous solution of dimethylamine.

On the basis of the literature [6] we should expect chloride (IV) to react with tertiary amines to give not compound (V), which would be expected in a normal reaction, but its isomer (VI) or a mixture of both. The structure of the salts obtained has not yet been elucidated.



$$CH_2{=}\overset{CH_3}{\overset{|}{C}}{-}CHCl{-}CH_3 \xrightarrow{R_3N} CH_3{-}CH{=}\overset{CH_3}{\overset{|}{C}}{-}CH_2{-}\underset{Cl}{NR_3}$$

(IV) (VI)

Results of cleavage of the prepared quaternary ammonium salts by aqueous caustic alkali are presented in the table.

Isoprene was identified by its physical constants and by the preparation of the dihydrochloride [3]; the tertiary amines were identified by the melting points of the picrates.

## EXPERIMENTAL

Quaternary ammonium salts were prepared by mixing equimolar quantities of alkyl halide and tertiary amine. The following procedure was used for cleavage of the ammonium salts: double the molar quantity of 40% aqueous sodium hydroxide was added gradually with stirring to the ammonium salt which was heated to 60-70° on a water bath. Heating was continued on a boiling water bath, during which operation the low-boiling products of cleavage (isoprene or vinylacetylene) were removed from the reaction mixture as soon as formed and collected in a receiver cooled with ice and salt. After distillation of the low-boiling product had ceased, the mixture was heated on a sandbath until the temperature of the evolved vapor had quickly risen to 70-75°; the objective of this measure was to extract the low-boiling products as completely as possible. The receiver was then changed, and the second component of the reaction (the amine) was distilled off from the reaction mixture. The amine layer was separated from the aqueous layer, dried and fractionally distilled.

1. Preparation of dimethyl-(α,β- or β,γ-dimethylallyl)-amine. An aqueous solution of sodium hydroxide was added to 9.95 g of dimethylbutynyl-(α,β- or β,γ-dimethylallyl) ammonium chloride heated to 65°. Vinylacetylene already started to come off at 68-70°. The cleavage reaction gave 8.4 g of vinylacetylene which distilled completely at 5.5-6° and gave a yellow precipitate with the Ilosvay reagent. The reaction mixture yielded 33.4 g (59.1%) of dimethyl-(α, β- or β,γ-dimethylallyl)-amine.

B. p. 111.5-117.5° (680 mm), $d^{20}_4$ 0.7731, $n^{20}D$ 1.4270, $MR_D$ 37.528; calculated 37.999.

Found %: N 12.49. $C_7H_{15}N$. Calculated %: N 12.39.

Picrate, m. p. 87-88°.

Found %: N 16.42. $C_{13}H_{18}O_7N_4$. Calculated %: N 16.37.

Methiodide, m. p. 139-140° [26].

2. Preparation of dimethyl-(γ,γ-dimethylallyl)-amine. A. An aqueous solution of sodium hydroxide was added to 17.2 g of dimethylbutynyl-(γ,γ-dimethylallyl) ammonium chloride. Cleavage took place at 79-80° and gave 2.6 g of vinylacetylene and 7.5 g (78.1%) of dimethyl-(γ,γ-dimethylallyl) amine.

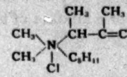
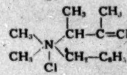
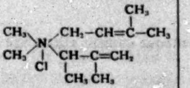
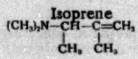
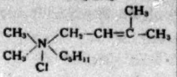
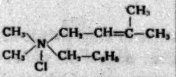
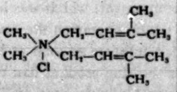
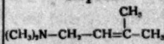
B. p. 116-118° (680 mm), $d^{20}_4$ 0.7711, $n^{20}D$ 1.4276, $MR_D$ 37.789: calculated 37.999.

Found %: N 12.21. $C_7H_{15}N$. Calculated %: N 12.39.

Picrate, m. p. 99-100°.

Found %: N 16.39. $C_{13}H_{18}O_7N_4$. Calculated %: N 16.37.

Methiodide, m. p. 160-161°.

| Quaternary salt | M. p. | Ionic Cl (in %) | | Products of cleavage by aqueous alkali | Yield (in %) | M. p. of amine picrate |
|---|---|---|---|---|---|---|
| | | found | calc. | | | |
|  | — | 16.37 | 16.17 | Isoprene<br>$(CH_3)_2N—C_5H_{11}$ | 65<br>72 | —<br>130° |
|  | 170—171° | 14.64 | 14.82 | Isoprene<br>$(CH_3)_2N—CH_2C_6H_5$ | 59<br>88 | —<br>96.5 |
|  | — | 15.91 | 16.32 | Isoprene<br> $(CH_3)_2N—\underset{CH_3}{\underset{\vert}{C}H}—\underset{CH_3}{\underset{\vert}{C}}=CH_2$ | 62<br>75 | —<br>87—88 |
|  | 90—92 | 15.90 | 16.17 | Isoprene<br>$(CH_3)_2N—C_5H_{11}$ | 58<br>67 | —<br>130 |
|  | 159—160 | 14.67 | 14.82 | Isoprene<br>$(CH_3)_2N—CH_2C_6H_5$ | 85<br>89 | —<br>96.5 |
|  | 110—111 | 16.27 | 16.32 | Isoprene<br> $(CH_3)_2N—CH_2—CH=\overset{CH_3}{\overset{\vert}{C}}—CH_3$ | 67<br>85 | —<br>99—100 |

B. 52.5 g of γ,γ-dimethylallyl chloride was stirred into 75 ml of 33% aqueous solution of dimethylamine. Heat was developed during the reaction. After the second layer had disappeared, a further 52 g of γ,γ-dimethylallyl chloride and 100 g of 40% aqueous sodium hydroxide was added. The aqueous layer was then subjected to cleavage by addition of 160 g of 50% sodium hydroxide solution. Cleavage took place at a temperature of 83-93° and gave 20 g of isoprene, which distilled completely at 29-32° (680 mm) (d$^{20}_{4}$ 0.6817, n$^{20}$D 1.4216) and 35 g of amine with b.p. 112-118°(600 mm);picrate with m. p. 99-100°. There was no depression of melting point of the mixture with the picrate of dimethyl-(γ,γ-dimethylallyl)-amine obtained by cleavage of dimethyl-(butyn-2-yl)--(γ,γ-dimethylallyl) ammonium chloride.

## SUMMARY

1. It was shown that quaternary ammonium salts obtained by interaction of α,β- and γ,γ-dimethylallyl chlorides with dimethylisoamyl-, dimethylbenzyl- and dimethyl-(γ,γ-dimethylallyl) amines are cleaved by hot aqueous alkali with formation of isoprene and the corresponding tertiary amine.

2. Cleavage of quaternary ammonium salts containing the butyn--2-yl radical in addition to the α,β- or γ,γ-dimethylallyl radical leads to formation of vinylacetylene. 1,4-Cleavage of the butyn-2-yl radical accordingly goes with greater facility than cleavage of the other radicals.

3. It was established that alkaline cleavage of dimethyl-(γ,γ-dimethylallyl)-(α,β- or β,γ-dimethylallyl) ammonium chloride leads to formation of isoprene at the expense of the γ,γ-dimethylallyl radical.

## LITERATURE CITED

[1] W. Euler, Ber. 30, 1989 (1897).

[2] Harries, Naresheimer, Lieb. Ann. 383, 173 (1911); German pat. 247144; Zbl. 1912, II, 159; German pat. 247145, 247271, 267040; Zbl. 1912, II, 72, 160; Zbl. 1913, II, 1905.

[3] I. L. Ostromyslenskii, J. Russ. Phys. Chem. Soc. 47, 1960, 1962, 1984 (1915).

[4] a) A. T. Babaian, N. G. Vartanian and I. Ia. Zurabov, J. Gen. Chem. 25, 1610 (1955);* b) A. T. Babaian and A. A. Grigorian, J. Gen. Chem. 26, 1945 (1956).*

[5] A. T. Babaian, G. M. Mkrian and I. Ia. Zurabov, Bull. Acad. Sci. USSR, Div. Phys. Math. and Nat. Sci. IX, 8, 25 (1956).

[6] D. V. Tishchenko, J. Gen. Chem. 6, 8, 1116 (1936); Meisenheimer and Link, Lieb. Ann. 479, 211 (1930); W. P. Young, I. D. Webb, U. L. Coering, J. Am. Chem. Soc. 73, 1076 (1951).

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# SUBSTITUTED HYDRAZIDES OF HYDROXYCARBOXYLIC ACIDS

## II. SYNTHESIS OF ARYLHYDRAZIDES OF DIALKYLGLYCOLIC ACIDS

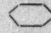
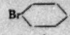
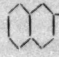
I. S. Berdinskii

The reaction of ethyl esters of β-arylhydrazides of oxalic acid with alkyl magnesium halides was studied in the course of development of the method described in the preceding communication [1]. Substances used were

$$Ar{-}NH{-}NH{-}CO{-}COOC_2H_5$$

where Ar = $C_6H_5$; p-$BrC_6H_4$ and β-$C_{10}H_7$; in the components RMgX, R = $C_2H_5$, $C_3H_7$, iso-$C_3H_7$, $C_4H_9$, iso-$C_5H_{11}$ and $C_8H_{17}$.

An experiment showed that reaction goes smoothly, and the arylhydrazides of dialkylglycolic acids are obtained in good yields. The structural formulas and melting points of the compounds that we obtained are given in the table. The synthesized arylhydrazides are colorless, crystalline substances, insoluble in water, soluble in common organic solvents; the arylhydrazides of acids with branched radicals are distinguished by higher melting points.

| Compound no. | Formula | Melting point |
|---|---|---|
| (II) | $-NH-NH-CO-C(OH)(C_2H_5)_2$ | 121—122.5° |
| (III) | $-NH-NH-CO-C(OH)(C_3H_7)_2$ | 122.5—123.5 |
| (IV) | $-NH-NH-CO-C(OH)(C_3H_7\text{iso})_2$ | 164—166 |
| (V) |  $-NH-NH-CO-C(OH)(C_4H_9)_2$ | 127—128.5 |
| (VI) | $-NH-NH-CO-C(OH)(C_5H_{11}\text{iso})_2$ | 173—174 |
| (VII) | $-NH-NH-CO-C(OH)(C_8H_{17})_2$ | 101—102 |
| (VIII) |  $-NH-NH-CO-C(OH)(C_4H_9)_2$ | 135—136 |
| (IX) |  $-NH-NH-CO-C(OH)(C_4H_9)_2$ | 152—154 |

## EXPERIMENTAL

Phenylhydrazide of diethylglycolic acid (II). 6.2 g of the ethyl ester of the β-phenylhydrazide of oxalic acid (I) was added to a solution of ethyl magnesium bromide prepared from 19.7 g of ethyl bromide and 4.4 g of magnesium. Finally, the reaction mass was heated on a water bath for 30 minutes and decomposed with dilute hydrochloric acid. The reaction product was extracted with ether. Yield 6.3 g (95.4%). Insoluble in water, soluble in ether, benzene, alcohol, toluene. Needles (from toluene), m. p. 121-122.5°.

Found %: N 12.83, 12.71. $C_{12}H_{18}O_2N_2$. Calculated %: N 12.61.

Phenylhydrazide of dipropylglycolic acid (III). Starting substances: 6.2 g of (I), 4.4 g of magnesium and 22.1 g of propyl bromide. Yield 7.1 g (95.3%). Sparingly soluble in ether and gasoline; more easily soluble in alcohol and toluene. Needles (from gasoline), m. p. 122.5-123.5°.

Found %: C 67.17, 67.02; H 8.77, 8.78; N 10.98, 10.91. $C_{14}H_{22}O_2N_2$. Calculated %: C 67.20; H 8.80; N 11.20.

Phenylhydrazide of diisopropylglycolic acid (IV). Starting substances: 2.1 g of (I), 1.4 g of magnesium and 4.7 g of isopropyl chloride. Yield 2.3 g (92%). Insoluble in gasoline, sparingly soluble in ether and dioxane; soluble in alcohol, toluene, glacial acetic acid, chloroform and carbon tetrachloride. Needles (from carbon tetrachloride), m. p. 164-166°.

Found %: N 10.91, 11.48. $C_{14}H_{22}O_2N_2$. Calculated %: N 11.20.

Phenylhydrazide of dibutylglycolic acid (V). Reactants were 6.2 g of (I), 24.7 g of butyl bromide and 4.4 g of magnesium. Yield 7.3 g (87.9%). Soluble in alcohol, benzene, gasoline and toluene. Prisms (from toluene), m. p. 127-128.5°.

Found %: N 9.82, 9.85. $C_{16}H_{26}O_2N_2$. Calculated %: N 10.07.

Phenylhydrazide of diisoamylglycolic acid (VI). Reaction was effected with 6.2 g of (I), 27.2 g of isoamyl bromide and 4.4 g of magnesium. Yield 8.3 g (91.21%). Sparingly soluble in ether, more readily soluble in toluene, alcohol and gasoline. Needles (from toluene), m. p. 173-174°.

Found %: N 8.80, 8.84. $C_{18}H_{30}O_2N_2$. Calculated %: N 9.15.

Phenylhydrazide of dioctylglycolic acid (VII). Starting substances: 5.5 g of (I), 31 g of n-octyl bromide and 3.9 g of magnesium. Yield 9 g (87.4%). Soluble in alcohol, ether, toluene and chloroform. Needles (from alcohol), m. p. 101-102°.

Found %: N 6.88, 7.29. $C_{24}H_{42}O_2N_2$. Calculated %: N 7.18.

p-Bromophenylhydrazide of dibutylglycolic acid (VIII). Reaction was effected with 2.9 g of the ethyl ester of the p-bromophenylhydrazide of oxalic acid, 8.4 g of butyl bromide and 1.5 g of magnesium. Yield 3.4 g (97.14%). Readily soluble in ether, more difficultly soluble in alcohol, toluene, and glacial acetic acid. Needles arranged in clusters (from toluene), m. p. 135-136°.

Found %: N 7.71, 7.62. $C_{16}H_{25}O_2N_2Br$. Calculated %: N 7.84.

β-Naphthylhydrazide of dibutylglycolic acid (IX). Starting substances: 2.0 g of the ethyl ester of the β-naphthylhydrazide of oxalic acid, 6.2 g of butyl bromide and 1.1 g of magnesium. Yield 2.3 g (92.0%). Insoluble in ether, soluble in toluene, alcohol and glacial acetic acid. Needles collected in clusters (from glacial acetic acid), m. p. 152-154°.

Found %: N 8.24, 8.39. $C_{20}H_{28}O_2N_2$. Calculated %: N 8.53.

## SUMMARY

The reaction between alkyl magnesium halides and esters of β-arylhydrazides of oxalic acid can be recommended for the preparation of arylhydrazides of dialkylglycolic acids. A series of previously undescribed representatives of this class of substances were prepared and their properties were studied.

## LITERATURE CITED

[1] I. S. Berdinskii and P. A. Petiunin, J. Gen. Chem. 26, 2592 (1956).*

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* Original Russian pagination. See C. B. Translation.

# SYNTHESIS OF SOME BIFUNCTIONAL COMPOUNDS CONTAINING SULFIDIC SULFUR

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Dinitriles, diamines and dicarboxylic acids containing sulfidic sulfur may be of interest as intermediates for production of polyamides, polyurethanes and polyethers. It is well-known that the synthesis of certain compounds of this group can be effected via δ-chlorovaleronitrile [1]. Information about these syntheses is inadequate. Syntheses and properties of the products are not described, but only preparative schemes are presented. The objective of the present investigation was to develop methods of synthesis of δ-chlorovaleronitrile, di-(4-nitrilotetramethylene) sulfide, di-(4-carboxytetramethylene) sulfide and di-(5-aminopentamethylene) sulfide.

## EXPERIMENTAL

δ-Chlorovaleronitrile. A mixture of 65 g of KCN, 254 g of 1,4-dichlorobutane and 200 g of adiponitrile was stirred at 135-140° for 10-12 hours. After cooling, the precipitate was filtered off, dissolved in water, and extracted from the water with benzene. The benzene solution was dried with calcined sodium sulfate and the benzene was distilled off. The residue was combined with the filtrate and fractionated in vacuo to give a 62% yield of product, calculated on the 1,4-dichlorobutane consumed.

B. p. 115-117° at 28 mm, $d^{20}_{20}$ 1.0536, $n^{20}$D 1.4430.

Found %: N 11.0. $C_5H_8NCl$. Calculated %: N 11.9.*

Di-(4-nitrilotetramethylene) sulfide. A mixture of 30 g of sodium sulfide nonahydrate, 45 g of δ-chlorovaleronitrile, 100 g of diethyleneglycol and 10 ml of water was heated to the boil (120°) and stirred at this temperature for 6 hours. After cooling, the precipitated NaCl was filtered off. The upper layer of liquid was collected from the filtrate, and the residue of reaction product was extracted from the lower layer with chloroform. After the chloroform had been driven off, the residue was combined with the separated upper layer of liquid, which contained di-(4-nitrilotetramethylene) sulfide, and distilled at 192-194° (3.5 mm). Yield 68% reckoned on the δ-chlorovaleronitrile consumed. The product was a yellowish liquid which gave the characteristic reaction for sulfur with sodium nitroprusside; $n^{20}$D 1.4863; $d^{20}_{20}$ 1.0230.

Found %: C 61.14; H 7.7; N 14.2. $C_{10}H_{16}N_2S$. Calculated %: C 61.2; H 8.1; N 14.2.

Di-(4-carboxytetramethylene) sulfide. A mixture of 24.5 g of di-(4-nitrilotetramethylene) sulfide and 100 ml of conc. HCl was heated on a boiling water bath for 4 hours and then poured into a porcelain beaker containing cold water; the acid came down in the form of crystals with m. p. 94-95°, acid number 478.3, calculated acid number 478.6. Yield 67%. A number of esters were prepared from the acid.

Di-(5-aminopentamethylene) sulfide. A solution of 20 g of di-(4-nitrilotetramethylene) sulfide in 200 ml of anhydrous ethanol was heated to the boil, and 40 g of sodium in small pieces was added at such a rate that the resulting foam did not disappear; the solution was then heated for 2 hours until the sodium had completely disappeared. After the mass had cooled, 200 ml of water was added to decompose the alcoholate; the alcohol was distilled off and the residual mixture separated into layers. The top layer was distilled under nitrogen in 2 ml portions at 146-148°. Yield 71.3%. The prepared di-(5-aminopentamethylene) sulfide is a colorless liquid; $n^{20}$D 1.5000; $d^{20}_{20}$ 1.0401.

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* According to [2], b. p. 115-118° at 28 mm; $n^{20}$D 1.4447; yield 48%.

Found %: C 59.5; H 12.6; N 13.55; $NH_2$ (Van Slyke method) 15.0. $C_{10}H_{24}N_2S$. Calculated %: C 58.8; H 11.7; N 13.7; $NH_2$ 15.6.

## SUMMARY

Methods were developed for the preparation of δ-chlorovaleronitrile, di-(4-nitrilotetramethylene) sulfide, di-(4-carboxytetramethylene) sulfide and di-(5-aminopentamethylene) sulfide.

## LITERATURE CITED

[1] W. Reppe, Kunststoffe, 40, 1 (1950); German pat. 70637; O. Cass, Ind. Eng. Ch. 40, 217 (1948).

[2] Nelson, Barthel, J. Am. Chem. Soc. 71, 3098 (1949).

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# TRANSFORMATION REACTIONS OF METHYLOLMETHACRYLAMIDE

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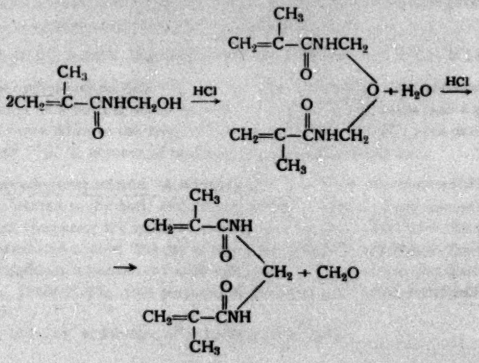
Feuer and Lynch were the first to synthesize unsaturated methylolamides by reacting acrylamide and methacrylamide with paraformaldehyde in either dichloroethane or carbon tetrachloride medium in the presence of a catalyst (colloidal sodium). When heated in organic solvents with hydrochloric acid the methylolmethacrylamide and methylolacrylamide were converted by them to methylene(bis)acrylamides [1]. According to existing literature data, certain methylolacyl- and arylamides served as model compounds in elucidating the complex mechanism of the reactions that take place in the condensation of urea with formaldehyde. Based on the data of Einhorn [2] and of Zigeuner [3], methylolamides in alkaline medium form diamidomethyl ethers, whereas the corresponding methylene compounds are formed under the influence of acids. Zigeuner and co-workers also expressed the theory that it is possible for diamidomethyl ethers to be formed in weakly acid medium [4].

In one of our experiments on the synthesis of methylolmethacrylamide by the method of Feuer and Lynch we isolated, together with the desired methylolmethacrylamide, a substance with m. p. 80.5-81.5°, which proved to be the previously unknown dimethacrylamidodimethyl ether. Repeated attempts made subsequently to again isolate this compound from the products of the indicated reaction for the synthesis of methylolmethacrylamide proved unsuccessful, which caused us to make a more detailed study of the transformation reactions of methylolmethacrylamide.

Attempts to synthesize dimethacrylamidodimethyl ether by reacting methylolmethacrylamide with benzoyl chloride in alkaline medium, similar to the procedure used by Zigeuner [5], proved unsuccessful. On the assumption that dimethacrylamidodimethyl ether should be formed as an intermediate product in the synthesis of methylenedimethacrylamide, we studied the behavior of methylolmethacrylamide in the presence of acid catalysts. When methylolmethacrylamide was heated with a small amount of hydrochloric acid it was converted to dimethacrylamidodimethyl ether. When the catalyst concentration was increased the dimethacrylamidodimethyl ether was converted to the previously known methylenedimethacrylamide



According to the data of Feuer and Lynch, methylolmethacrylamide when heated in the presence of mineral acids and boron trifluoride is polymerized to infusible and insoluble polymers, which is evidence of their tridimensional structure. Our experiments on the matter revealed that methylolmethacrylamide is also polymerized under the influence of peroxide initiators, and here, depending on the polymerization conditions, it is possible to obtain either linear or tridimensional polymers. When exposed to ultraviolet radiation methylolmethacrylamide is polymerized to an infusible solid. Bulk polymerization in the presence of benzoyl peroxide yields a glassy polymer, insoluble in water and the common organic solvents. Polymerization in aqueous medium permits obtaining a linear polymer that is soluble in water, glycol and glycerin.

## EXPERIMENTAL

Methacrylamide (I) was obtained by a modification of the Arcus method [6]. Instead of the tedious operation of isolating (I) from dilute aqueous ammonia solution by steam-distillation under reduced pressure, we cooled the homogeneous reaction mixture to −40°. The obtained crystals of (I) were filtered and dried at 50-60°. The yield of (I) (m. p. 108-110°) was 67-70%. The obtained (I) can we used without further purification for the synthesis of methylolmethacrylamide.

Preparation of catalysts. Sodium metal was converted to thin sheets under xylene. Sodium ethylate was used as a finely divided powder.

Methylolmethacrylamide (II). a) Synthesis by the method of Feuer and Lynch [1]. The results of the experiments made to study the influence of the amount of catalyst on the reaction rate are summarized in the table. In all of the experiments the amount of (I) taken was 71 g (in 1 liter of carbon tetrachloride), and the bath temperature was 45-50°.

Influence of the Amount of Catalyst on the Formation Rate of Methylolmethacrylamide

| Catalyst | Amount (in %) | Reaction time (in minutes) |
|---|---|---|
| Sodium metal | 0.1 | 60 |
| | 0.2 | 45 |
| | 0.3 | 30 |
| | 0.4 | 18 |
| Sodium ethylate | 0.5 | 30 |
| | 1.0 | 3-5 |
| | 1.5 | 0.5-1 |

From the data given in the table it can be seen that the formation rate increases with increase in the amount of catalyst.

b) The reaction was run in toluene with 1.5% of catalyst (sodium ethylate). On conclusion of reaction, which took 15 minutes, we isolated (II) in 64% yield from the reaction mixture.

Dimethacrylamidodimethyl ether (III). A mixture of 40 g of (II) and 200 ml of dichloroethane, the latter containing 0.14 g of hydrochloric acid, was heated with stirring for 70 minutes at 45-50°. After removal of the solvent and two recrystallizations from benzene we obtained crystals with m. p. 80.5-81.5°. Yield of (III) 16 g (43.4%).

Found %: C 56.50; H 7.6; N 13.18. M 212.6. $C_{10}H_{16}O_3N_2$. Calculated %: C 56.56; H 7.6; N 13.2. M 212.14.

The tetrabromide was analyzed for bromine.

Found %: Br 60.08. $C_{10}H_{16}O_3N_2Br_4$. Calculated %: Br 60.09.

Methylenedimethacrylamide (IV). A mixture of 4 g of (III) and 20 ml of dichloroethane, the latter containing 1.4 g/liter of hydrochloric acid, was heated at 60° for 5 hours. On conclusion of reaction a precipitate of 0.6 g of crystals deposited from the reaction mixture. Removal of the solvent yielded 2.8 g of (IV) with m. p. 161-164°. Yield 81.6%. Methylenedimethacrylamide melts at 162-163° [1].

Polymerization of (II). a) Under the influence of ultraviolet light. We used a PRK-2 lamp as the light source. The wavelength region in the vicinity of λ ~ 3000 A was used for the polymerization. 1.5 g of (II) with m. p. 53.5-54.5° (% N 12.18) was placed on a watch glass at a distance of 50 cm from the light source. Irradiation at 35° was maintained for 19 hours. At the end of reaction the polymer was purified by extraction with ethyl acetate. After drying we obtained 1.204 g (80.3%) of a polymer, insoluble in water and organic solvents (% N 12.14).

b) In solvent. Ten grams of (II) was dissolved in 100 ml of water, containing 0.075 mole/liter of hydrogen peroxide. The mixture was heated with stirring at 60-70° in a stream of carbon dioxide for 7 hours. At the end of heating a viscous solution of the polymer was obtained. The polymer was isolated from solution by precipitation in methyl alcohol. The precipitate was filtered and dried to give 5.3 g (53%) of a cottony polymer. The polymer is soluble in water, glycol and glycerin, and shows slight swelling in pyridine. Its characteristic viscosity, determined in an Ostwald viscosimeter, is 0.41.

## SUMMARY

1. The behavior of methylolmethacrylamide under the influence of acid catalysts was studied. We were the first to synthesize and characterize dimethacrylamidodimethyl ether, which was converted to methylenedimethacrylamide when the concentration of the catalyst was increased.

2. The polymerization of methylolmethacrylamide in aqueous solution using an initiator (hydrogen peroxide) gave a linear polymer.

## LITERATURE CITED

[1] H. Feuer, U. Lynch, J. Am. Chem. Soc. 75, 5027 (1953).

[2] A. Einhorn, Lieb. Ann. 343, 207 (1905).

[3] G. Zigeuner, K. Voglar, R. Pitter, Monatsh. 85, 1196 (1954).

[4] G. Zigeuner, Kunststoffe 41, 221 (1951).

[5] G. Zigeuner, W. Knierzinger, K. Voglar, Monatsh. 82, 847 (1951).

[6] C. L. Arcus, J. Chem. Soc. 1949, 2732.

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# OXIDATION OF α,β-UNSATURATED METHYL KETONES WITH SODIUM HYPOBROMITE

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The oxidation of α,β-unsaturated methyl ketones with hypohalites is a method that is used for the preparation of certain α,β-unsaturated acids. Unsaturated ketones of the alkyl aryl series are converted to the corresponding unsaturated acids in yields up to 88% [1, 2]. The data existing in the literature on the oxidation of α,β-unsaturated ketones of the aliphatic series relate to ketones with a branched chain of carbon atoms; the yields of unsaturated acids in this case range from 23 to 49% [3-6].

When the indicated reaction was applied to α,β-unsaturated methyl ketones with a straight carbon chain, and specifically to 3-nonen-2-one and 3-decen-2-one, we obtained the corresponding α,β-unsaturated acids, also in a yield of about 40%. Together with this, we also established that α,β-dihydroxy acids are formed here (α,β-dihydroxycaprylic acid in 10% yield and α,β-dihydroxypelargonic acid in 20% yield, respectively). Variation in the reaction conditions, such as changing the caustic concentration (from 0.2 to 2%), the amount of active bromine (from 3 to 8%), and also the temperature (from 10 to 70°), exerts very little influence on the formation of the dihydroxy acids.

The formation of the corresponding α,β-dihydroxy acids was also observed when other α,β-unsaturated ketones with a straight carbon chain were oxidized. Thus the oxidation of 3-undecen-2-one and 3-tridecen-2-one gave respectively α,β-dihydroxydecanoic acid in 10% yield and α,β-dihydroxydodecanoic acid in 20% yield. The yield of the α,β-unsaturated acids was about 30%.

In view of the fact that the formation of dihydroxy acids was not observed in the above mentioned studies on the oxidation with hypohalites of α,β-unsaturated methyl ketones of the aliphatic series with a branched chain, we repeated some of these experiments. We were unable to establish the presence of dihydroxy acids in the reaction mixture when either mesityl oxide or 5-methyl-3-hexen-2-one was oxidized with sodium hypobromite. This makes it possible to assume that the presence of branching near the double bond in the molecule of the starting ketone makes the formation of dihydroxy acids in the discussed reaction difficult.

The formation of α,β-dihydroxy acids when α,β-unsaturated ketones are oxidized with hypobromite is probably due to the hydration of the initially obtained glycidic acids. For example, it is indicated that a glycidic acid is formed when cinnamaldehyde is oxidized with sodium hypobromite [7]. Other evidence in support of this is the fact that all of the α,β-dihydroxy acids obtained by us proved to have different melting points from the α,β-dihydroxy acids formed in the oxidation of the corresponding α,β-unsaturated acids with permanganate, but identical with the melting points of the dihydroxy acids obtained from the glycidic acids. Thus, the α,β-dihydroxy acid isolated by us from the oxidation of 3-decen-2-one with sodium hypobromite had the same melting point (116°) as the dihydroxy acid obtained in the oxidation of α,β-nonenoic acid with performic acid [8]. This same acid was obtained by us when we subjected the ethyl ester of hexylglycidic acid, synthesized by the Darzens method [9], to hydration and then hydrolysis.

The oxidation of α,β-unsaturated methyl ketones can be depicted by the scheme shown on page 1329.

#### TABLE 1

Properties of Unsaturated Ketones

| Name of ketone | Yield (in %) | B. p. (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ |  | Amt. of ketone (in %)* | Bromine no. |  | M. p. of derivatives |  | N content in derivatives (in %) |  | Remarks |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  | found | calc. |  | found** | calc. | semicarbazone | 2,4-dinitrophenylhydrazone | found | calc. |  |
| Benzalacetone*** | 63.7 | 128–133° (10) | — | — | — | — | 99.3 | 108 | 109 | — | — | — | — | — |
| Mesityl oxide | — | 129–133 | 1.4480 | — | — | — | — | 171 | 163 | — | — | — | — | Commercial product used |
| 5-Methyl-3-hexen-2-one | 54.2 | 65—68 (13) | 1.4380 | 0.8545 | 34.34 | 34.07 | 100 | 150 | 142 | 125.5° | — | 24.65,<br>24.50 | 24.84 | — |
| 3-Nonen-2-one | 70 | 72 (6) | 1.4470 | 0.8478 | 44.09 | 43.30 | 100 | 120 | 113 | 116—117 | — | 21.25,<br>21.36 | 21.32 | New |
| 3-Decen-2-one | 74 | 82—85 (5) | 1.4480 | 0.8474 | 48.64 | 47.92 | 99.2 | 111 | 103 | 117—118 | — | 19.51,<br>19.65 | 19.90 | — |
| 3-Undecen-2-one | 59 | 98—99 (5) | 1.4485 | 0.8631 | 52.15 | 52.54 | 92 | 87 | 95 | — | 73° | 16.35,<br>16.41 | 16.09 | New |
| 3-Tridecen-2-one | 65 | 106 (6) | 1.4522 | 0.8513 | 62.16 | 61.77 | 105 | 86 | 81 | — | 75 | 15.09,<br>14.81 | 14.89 | New |

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* Determined by the oximation method of L. N. Petrova and E. N. Novikova [12].

** Determined by the Kaufmann method.

*** Obtained by the condensation of benzaldehyde with acetone in the presence of 10% aqueous NaOh solution [13].

TABLE 2

Properties of Unsaturated Acids

| Starting ketone | Name of unsaturated acids | Yield (in %) | Boiling point (pressure in mm) | $n^{20}_D$ | $d^{20}_4$ | $MR_D$ |  | Acid Number |  | Bromine number (Kaufmann method) |  |
|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  | Found | Calc. | Found | Calc. | Found | Calc. |
| Mesityl oxide | Dimethylacrylic | 44 | M. p. 68.5-69.5° | — | — | — | — | 559.2 | 560 | 161.3 | 160 |
| 5-Methyl-3-hexen-2-one | Isohexenoic | 72 | 98 (6) | 1.4490 | 0.9527 | 32.06 | 30.97 | 489 | 491 | 130 | 140 |
| 3-Nonen-2-one | $\Delta^2$-Octenoic | 42.5 | 130-131 (6) | 1.4588 | 0.9442 | 41.00 | 40.21 | 392 | 394 | 108 | 112 |
| 3-Decen-2-one | $\Delta^2$-Nonenoic | 36.8 | 134-136 (4) | 1.4600 | 0.9385 | 45.32 | 44.83 | 355 | 359 | 94 | 102 |
| 3-Undecen-2-one | $\Delta^2$-Decenoic | 33 | 147-148 (8) | 1.4610* | 0.9365* | 49.75 | 49.44 | 328 | 329 | 87.8 | 94 |
| 3-Tridecen-2-one | $\Delta^2$-Dodecenoic | 21 | 141-142 (3) | 1.4615 | 0.9265 | 58.70 | 58.68 | 292 | 282 | 80.1 | 80.8 |

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* The determinations were made at 23°

TABLE 3

Properties of $\alpha,\beta$-Dihydroxy Acids, Obtained in the Oxidation of Unsaturated Methyl Ketones with Hypobromite

| Name of acids | Melting point | Literature melting point for dihydroxy acids obtained from corresponding unsaturated acids |  | Acid number |  | Amount of hydroxyl (in %) |  | Elemental analysis (in %) |  |  |  |  |  | Yields of dihydroxy acids (in %) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  |  |  | of dihydroxy acid |  |  |  | of silver salt |  |  |
|  |  |  |  |  |  |  |  | Found |  | Calc. |  | Found | Calc. |  |
|  |  | By oxidation with potassium permanganate | By oxidation with per-acids | Found | Calc. | Found* | Calc. | C | H | C | H | Ag | Ag |  |
| $\alpha,\beta$-Dihydroxyoctanoic | 114-115° | 118-119° [14] | – | 318 | 314 | 28 | 28.63 | 53.84,<br>53.90 | 9.12, 9.08 | 53.93 | 8.98 | 38.18 | 38.00 | 10.0 |
| $\alpha,\beta$-Dihydroxypelargonic | 116-117°** | 123 [15] | 118° [8] | 300 | 295 | 27.1 | 26.84 | 56.65,<br>56.25 | 9.52, 9.42 | 56.84 | 9.47 | 36.26 | 36.20 | 20.0 |
| $\alpha,\beta$-Dihydroxydecanoic | 108-110 | 121-123 [16] | – | 278.6 | 274 | 16.24 | 25.0 | 58.35,<br>58.35 | 9.72, 9.78 | 58.88 | 9.80 | – | – | 10.4 |
| $\alpha,\beta$-Dihydroxydodecanoic | 108-109 | 123 [17] | – | 245 | 241 | 18.6 | 21.9 | 61.27,<br>61.26 | 10.00,<br>10.17 | 62.00 | 10.34 | – | – | 20.0 |

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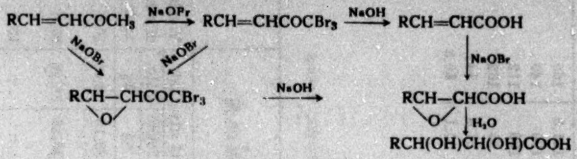
* Determined by the Zerevitinov method. The poor agreement of the results in the last two cases is apparently due to the poor solubility of the dihydroxy acids in xylene and diisobutyl ether.

** The mixed melting point with the dihydroxy acid obtained from the hydration and hydrolysis of the hexylglycidic acid ester was not depressed. The mixed melting point with the acid obtained from the oxidation of the nonenoic acid with potassium permanganate was 97-99°.



## EXPERIMENTAL

The unsaturated ketones were obtained by the V. I. Esafov method [10], i.e., by the condensation of the corresponding aldehydes with acetone in the presence of piperidine and glacial acid. The properties of the unsaturated ketones are listed in Table 1.

Oxidation of unsaturated ketones with sodium hypobromite. Sodium hypobromite* (containing 5-7% active bromine and 1-1.5% sodium hydroxide), taken in 20% excess, was added with vigorous stirring to the unsaturated ketone at 35-40°. Then the reaction mixture was kept at 28-35° for 3-4 hours; the excess hypobromite was destroyed with bisulfite solution, and the alkaline solution was first extracted with diethyl ether and then acidified with concentrated hydrochloric acid until acid to Congo. The product obtained on acidification was separated and steam-distilled, in which connection the unsaturated acid came over in the distillate, while the α,β-dihydroxy acid remained in the distillation flask. The unsaturated acids were isolated from the distillate in conventional manner and then vacuum-distilled; the α,β-dihydroxy acids were extracted with ether, and after removal of the solvent, were purified by washing with either cyclohexane or petroleum ether. The properties of the obtained α,β-unsaturated acids and α,β-dihydroxy acids are given in Tables 2 and 3.

Preparation of α,β-dihydroxypelargonic acid by the Darzens method. The condensation of enanthole with ethylmonochloroacetate was run in conventional manner. The yield of ethyl hexylglycidate was 18.6%.

B. p. 122-123° (7 mm), $n^{20}D$ 1.4450, $d^{20}_4$ 0.9828.

Literature [9]: b. p. 117-119° (6 mm); $n^{20}D$ 1.4448, $d^{20}_4$ 0.9882.

The glycidic acid ester (19 g) was refluxed for 3 hours with 60 g of 10% NaOH solution. The alkaline solution was first extracted with ether and then acidified. The acid that separated here was extracted with ether; the ether extract was worked up in conventional manner. After removal of the solvent we obtained 7 g of crystalline α,β-dihydroxypelargonic acid with m. p. 101-105°. Yield 38.8%. After washing with cyclohexane the acid had m. p. 115-116°, acid number 295 (calcd. 294), and content of hydroxyl groups 26.1% (calcd. 26.8%). Its mixed melting point with the α,β-dihydroxypelargonic acid obtained by us from the oxidation of 3-decen-2-one with sodium hypobromite was not depressed.

## SUMMARY

It was shown that the oxidation of aliphatic α,β-unsaturated methyl ketones of normal structure with sodium hypobromite yields, together with α,β-unsaturated acids, the corresponding α,β-dihydroxy acids. The formation of dihydroxy acids was not observed when methyl ketones, having a branched chain near the ethylenic bond, were oxidized.

It was established that the obtained dihydroxy acids are different from the α,β-dihydroxy acids formed in the oxidation of unsaturated acids with potassium permanganate, but are identical with the dihydroxy acids obtained in the hydration of the corresponding glycidic acids.

## LITERATURE CITED

[1] J. Wegmann, H. Dahn, Helv. Chim., Acta 29, 101 (1946).

---

* Obtained by the addition of bromine to aqueous sodium hydroxide solution [11].

[2] Organic Syntheses [Russian translation] Coll. Vol. 2, p. 351 (1949).

[3] Th. White, J. Chem. Soc. 1943, 238.

[4] S. G. Powell, D. A. Ballard, J. Am. Chem. Soc. 60, 1914 (1938).

[5] Organic Syntheses [Russian translation] Coll. Vol. 3, p. 182 (1952).

[6] S. David, C. Imer, Bull. Soc. Chim. 1951, 634.

[7] J. Colonge, E. Le Sech and R. Marey, Bull. Soc. Chim. France 1956, 813 [C.A. 51, 1090 (1957)].

[8] J. English, J. Gregory, J. Am. Chem. Soc. 69, 2120 (1947).

[9] V. F. Martynov and G. Ol'man, J. Gen. Chem. 25, 1561 (1955).*

[10] V. I. Esafov, J. Gen. Chem. 13, 814 (1943).

[11] A. P. Salchinkin and L. B. Lapkova, J. Appl. Chem. 29, No. 1, 141 (1956).*

[12] E. N. Novikova and L. N. Petrova, J. Appl. Chem. 23, 1336 (1950).*

[13] Organic Syntheses [Russian translation] Coll. Vol. 1, p. 76 (1949).

[14] F. L. Breusch, F. Baykut, Rev. faculte sci. univ. Istanbul 16a, 137 (1951); Ch. A. 6867 (1953).

[15] W. Krohs, Ber. pharm. Ges. 32, 336 (1922); Zbl. 1923, I, 819.

[16] F. L. Breusch, R. Tulus, Rev. Faculte sci. univ. Istanbul, 12a, 289 (1947); Ch. A. 6752a (1948).

[17] D. R. Koolhaas, Rec. trav. chim. 51, 460 (1932); Zbl. 1932, II, 630. [C.A. 26, 3788 (1932)].

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* Original Russian pagination. See C. B. Translation.

# SYNTHESIS OF SOME ESTERS OF 4,4'-DIHYDROXYDIPHENYL SULFONE AND CARBOXYLIC ACIDS

S. N. Baranov, F. A. Zhoglo and R. V. Visgert

A number of sulfone derivatives have proved to be highly active toward acid-resistant microorganisms, especially those responsible for tuberculosis and leprosy. Thus, at the present time 4,4'-diaminodiphenyl sulfone is the preferred agent used in the treatment of leprosy in French Guiana.

Much less attention has been devoted to the hydroxy derivatives of diphenyl sulfone, although these could be expected to show bactericidal action. According to [1], 4,4'-diamono-2,2'-dihydroxydiphenyl sulfone shows in vitro antibactericidal activity toward M. tuberculosis, streptococci, B. pyogenes, B. coli and staphylococci. Diacetyldihydroxydiphenyl sulfone can be used in the treatment of bacterial infections (miningococci and gonococci) [2].

Our objective was to synthesize some neutral esters of 4,4'-dihydroxydiphenyl sulfone with various carboxylic acids of the aliphatic, aromatic and heterocyclic series. Statements exist in the literature that esters of 4,4'-dihydroxydiphenyl sulfone are obtained by the condensation of the latter with acids in the presence of phosphorus oxychloride [3]. We utilized the same method. The compounds needed for the syntheses were either purchased or synthesized by us using the methods described in the literature, and were checked for purity by determining the chemical constants, and in some cases also by analysis. To synthesize the esters we took dry dihydroxydiphenyl sulfone and ground it intimately in a mortar with the proper acid (1 part of sulfone and 2 parts of acid), after which the mixture was transferred to a flask and heated in a glycerin bath at 120-140°; then the calculated amount of phosphorus oxychloride was cautiously added in drops. After all of the phosphorus oxychloride had been added the melt was heated until hydrogen chloride ceased to evolve. Then the melt was cooled and treated with 5% soda solution; this resulted in the removal of both organic and inorganic acids, and also of unreacted dihydroxydiphenyl sulfone. The ester that remained was purified by recrystallization.

The ester of α-bromoisovaleric acid and dihydroxydiphenyl sulfone was obtained by heating α-bromoisovaleryl bromide with the sodium salt of dihydroxydiphenyl sulfone.

The obtained esters are either white or light-yellow powders, difficultly soluble in water, and soluble in alcohol, acetone and dioxane. The ester of the sulfone and nicotinic acid is readily soluble in dilute hydrochloric acid. The esters suffer hydrolysis when heated with 10% aqueous caustic solution. They are hydrolyzed in the cold with alcoholic caustic.

The properties of the 14 esters obtained by us are given in the Table.

## EXPERIMENTAL

4,4'-Dihydroxydiphenyl sulfone. One gram-mole of p-hydroxybenzenesulfonic acid was placed in a flask and then 13 ml of 98% sulfuric acid and 1 g-mole of phenol were added. The temperature was raised rapidly to 165° and the mixture kept at this temperature for 6 hours. Then the temperature was raised to 195-200° and heated for another 6 hours. The mixture was cooled and the precipitate was recrystallized three times from hot water. M. p. 238-239° (literature [4]: m. p. 240-241°). Yield 80-85%.

Diacetyl-p-aminosalicylic acid. Five grams of the sodium salt of p-aminosalicyclic acid was dissolved at the boil in a mixture of 250 ml of benzene and 20 ml of acetic anhydride. The mixture was refluxed for 4

Esters of 4,4'-Dihydroxydiphenyl Sulfone and Carboxylic Acids $RCOOC_6H_4SO_2C_6H_4OOCR$

| R | Empirical formula of ester | Recrystallization solvent* | Yield (in %) | External appearance** | Melting point | S content (in %) | |
|---|---|---|---|---|---|---|---|
| | | | | | | found | calc. |
| n.-$C_4H_9$ | $C_{22}H_{26}O_6S$ | al | 50—55 | wc | 88—89° | 7.95 | 7.68 |
| α-$C_4H_8Br$ | $C_{22}H_{24}O_6SBr_2$ | d | 32—35 | wc | 73—74 | 5.22 | 5.55 |
| o-$CH_3COOC_6H_4$ | $C_{30}H_{22}O_{10}S$ | al | 87—90 | wp | 288—290 | 5.23 | 5.57 |
| p-$CH_3COOC_6H_4$ | $C_{30}H_{22}O_{10}S$ | al | 85—90 | wp | 300 | 5.17 | 5.57 |
| $C_6H_5CH=CH$ | $C_{30}H_{22}O_6S$ | d | 85—90 | wp | 270—273 | 6.43 | 6.27 |
| m-$O_2NC_6H_4CH=CH$ | $C_{30}H_{20}O_{10}N_2S$ | d | 85—90 | wp | 202—205 | 5.65 | 5.33 |
| $C_6H_5CHBrCHBr$ | $C_{30}H_{22}O_6Br_4S$ | al | 85—90 | wp | 170—172 | 4.34 | 3.86 |
| $C_6H_5CH_2CH_2$ | $C_{30}H_{26}O_6S$ | al | 85—90 | wp | 180—182 | 5.89 | 6.20 |
| $C_6H_5CONHCH_2$ | $C_{30}H_{24}O_8N_2S$ | ac | 80—85 | wp | 238—240 | 5.66 | 5.59 |
| o-$CH_3CONHC_6H_4$ | $C_{30}H_{24}O_8N_2S$ | d | 50—55 | y | 208—210 | 5.22 (N) | 4.88 (N) |
| m-$CH_3CONHC_6H_4$ | $C_{30}H_{24}O_8N_2S$ | d | 50—55 | y | 195—197 | 4.63 (N) | 4.88 (N) |
| p-$CH_3CONHC_6H_4$ | $C_{30}H_{24}O_8N_2S$ | d | 50—55 | y | 216—219 | 5.11 (N) | 4.88 (N) |
| $C_5H_4N$ | $C_{24}H_{16}O_6N_2S$ | ac | 85—90 | y | 203—204 | 7.05 | 6.95 |
| $\left.\begin{array}{l}4(CH_3CONH)\\2(CH_3COO)\end{array}\right\rangle C_6H_3$ | $C_{34}H_{28}O_{12}N_2S$ | d | 51—55 | y | 155—158 | 3.96 (N) | 4.06 (N) |

* al — alcohol, d — dioxane, ac — acetone.

** wp — white powder, wc — white crystals, y — yellow powder.

hours. Crystals of diacetyl-p-aminosalicyclic acid deposited on cooling. M. p. 286-288° (from a mixture of benzene and dioxane in a 5:1 ratio).

Found % N 6.25, 6.11. $C_{11}H_{11}O_5N$. Calculated % N 5.90.

The acetyl derivatives of the o-, m- and p-aminobenzoic acids were obtained in a similar manner.

Ester of dihydroxydiphenyl sulfone and α-bromoisovaleric acid. A mixture of 1.47 g of the sodium salt of dihydroxydiphenyl sulfone and 2.45 g of α-bromoisovaleryl bromide was heated in a glycerin bath at 110-130° for 2 hours. The melt after cooling was treated with 1% soda solution, and then with hot water. The crude ester was recrystallized from a small volume of dioxane. Yield 0.8 g. M. p. 73-74°.

Ester of dihydroxydiphenyl sulfone and cinnamic acid. A mixture of 2.5 g of dihydroxydiphenyl sulfone and 2.96 g of cinnamic acid was intimately ground in a mortar and then heated in a flask in a glycerin bath at 120-140°; then the phosphorus oxychloride (0.8 ml) was added in drops. Heating was continued until hydrogen chloride ceased to evolve (3-3.5 hours). The melt after cooling was treated with 5% soda solution; this made it possible to remove both inorganic and organic acids, and also unreacted dihydroxydiphenyl sulfone. The ester was purified by recrystallization from dioxane. White crystalline powder; m. p. 271-272°.

The other esters of acids and dihydroxydiphenyl sulfone were obtained in a similar manner. The obtained esters proved to be inactive toward staphylococci (both white and golden), dysentery bacillus, diphtheria bacillus and capsule microbes. The ester of diacetyl-p-aminosalicyclic acid and dihydroxydiphenyl sulfone shows slight in vitro activity against tubercle bacillus.*

## SUMMARY

We synthesized and characterized the neutral esters of 4,4'-dihydroxydiphenyl sulfone and the acids: valeric, α-bromoisovaleric, p- and o-acetoxybenzoic, o-, m- and p-acetamidobenzoic, cinnamic, m-nitrocinnamic, phenylpropionic, dibromophenylpropionic, hippuric, nicotinic and diacetyl-p-aminosalicyclic.

## LITERATURE CITED

[1] W. Linnell and J. Stenlake, J. Pharm. Pharmacol. 2, 937 (1950).

---

* The testing was done in the Microbiology Department of the S. M. Kapustiak L'vov Medical Institute.

[2] C. Levaditi, A. Girard and A. Vaisman, C. A. 32, 3022 (1938).

[3] Ia. P. Berkman and R. V. Vizgert, Ukrain. Chem. J. 17, 270 (1951).

[4] L E. Hinkel and G. H. Ralph Summers, J. Chem. Soc. 1949, 2854.

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# CYCLOALKYLATION OF AROMATIC COMPOUNDS

## XIV. CONDENSATION OF CYCLOHEXANOL WITH SOME AROMATIC HYDROCARBONS

N. G. Sidorova and I. A. Poliker

Continuing our investigations on the alkylation of aromatic compounds with cyclic alcohols [1], we studied the condensation of the xylenes, mesitylene, naphthalene and fluorene with cyclohexanol in the presence of aluminum chloride.

The cyclohexylation of the xylenes has received little study. The first paper on this subject describes the condensation of m-xylene with cyclohexyl bromide in the presence of ferric chloride [2]. Later Bodroux [3], who studied the alkylation of aromatic compounds with cyclohexene in the presence of aluminum chloride, obtained the cyclohexyl derivatives of a large number of hydrocarbons, including those of m- and p-xylene. Recently the cyclohexyl ester of p-toluenesulfonic acid has been used to cyclohexylate m- and p-xylene [4].

The only method used to introduce the cyclohexyl group into mesitylene was by condensing the latter with cyclohexene in the presence of aluminum chloride [3].

Various methods have been used to cyclohexylate naphthalene. Bodroux [5] condensed naphthalene with cyclohexene and obtained 19% of mixed cyclohexylnaphthalenes, containing predominantly the β-isomer, and 2,6-dicyclohexylnaphthalene. A similar reaction is described in an American patent [6]. Pokrovskaia and Stepantsova [7] employed the Bodroux method and, depending on the ratios of the reactants, obtained products with a variable amount of mono- and polycyclohexylnaphthalenes (up to the tetra-substituted derivative). Later Buu-Hoi and Cagniant [8] employed the same method to obtain 2,6-dicyclohexylnaphthalene. The condensations of naphthalene with cyclohexene and cyclohexanol in the presence of boron fluoride are also described [9, 10]. The best yield (63%) of β-cyclohexylnaphthalene was obtained with cyclohexanol. Of interest is the fact that the disubstituted product obtained in the presence of boron fluoride has the structure of 1,4-dicyclohexylnaphthalene, whereas the 2,6-isomer is formed with aluminum chloride [11].

Of special interest is the condensation of cyclohexanol with fluorene, since the nuclear alkylation of fluorene has hardly been studied. Only three papers on this subject are known – the condensation of fluorene with benzyl chloride in the presence of zinc [12], the alkylation of fluorene with propylene in the presence of phosphoric acid [13], and the reaction of fluorene with some olefins and alkyl chlorides [14].

To avoid side reactions we ran the alkylation of the xylenes, mesitylene and naphthalene with cyclohexanol using the minimum amount of aluminum chloride, a large excess of the hydrocarbon, and a low temperature.

In the case of mesitylene the best results were obtained with 0.7 g-equiv. of aluminum chloride (based on cyclohexanol), and in the remaining cases with 0.82-0.84 g-equiv.

We obtained 4-cyclohexyl-1,2-dimethylbenzene in 71.5% yield from o-xylene. The reaction was somewhat poorer with p-xylene; under similar conditions the yield of 2-cyclohexyl-1,4-dimethylbenzene was 68.6%. The alkylation of m-xylene went with extreme ease, and an 86% yield of 5-cyclohexyl-1,3-dimethylbenzene was obtained from it. The structure of this product was shown by its oxidation to trimesic acid, which was then converted to the trimethyl ester. Previous investigators [2, 3] also obtained the same hydrocarbon from m-xylene. However, in a recent paper [15] the structure of 4-cyclohexyl-1,3-dimethylbenzene is assigned to the condensation product of m-xylene with cyclohexene in the presence of aluminum chloride.

The condensation of mesitylene with cyclohexanol gave a 35.9% yield of 2-cyclohexyl-1,3,5-trimethylbenzene. However, this yield is not lower than that obtained in the condensation of mesitylene with cyclohexene [3].

The alkylation of naphthalene gave about a 59% yield of a monocyclohexylnaphthalene fraction, composed mainly of the β-isomer, and about a 40% yield of a dicyclohexylnaphthalene fraction, in which the presence of the 2,6-isomer was shown.

A comparison of the obtained results with literature data, in addition, shows that cyclohexanol is the most convenient alkylating agent for the introduction of the cyclohexyl radical into aromatic compounds. The yields obtained with it are frequently higher than those obtained with either cyclohexene or cyclohexyl chloride, and the reaction products do not contain polymeric impurities, which is the case when cyclohexene is used.

The condensations of fluorene with cyclohexanol proceed with considerable difficulty. An excess of the hydrocarbon being alkylated leads to a reduction in the yield in this case. For this reason the reactions were run either with equimolar amounts of fluorene and cyclohexanol or with an excess of the latter. The aluminum chloride was taken in an amount of 0.85 g-equiv. based on the cyclohexanol. The maximum yield of crude cyclohexylfluorene obtained by us under these conditions was 37%, calculated on the weight of fluorene taken for reaction. However, a part of the fluorene remains unchanged here and can be recycled.

Although the use of excess cyclohexanol leads to an increased yield of cyclohexylfluorene, still the product obtained in such case is less pure than when equimolar amounts of the reactants are taken.

## EXPERIMENTAL

The condensations were run in conventional apparatus, without a stirrer. The aluminum chloride was slowly added in small portions to the mixture of hydrocarbon and cyclohexanol; the mixture was shaken periodically. In the case of naphthalene and fluorene the reactions were run in a solution of dearomatized petroleum ether. (The aromatics were removed from the petroleum ether by chromatographic adsorption on silica gel.) After all of the aluminum chloride had been added the mixture was allowed to stand overnight, and then it was heated on the water bath. The mixture after cooling was decomposed with dilute hydrochloric acid, and the hydrocarbon layer was dried over calcium chloride and distilled from sodium. The liquid reaction products were redistilled from sodium. The results of the different condensations are summarized in the Table.

Conditions and Results of the Condensations

| Aromatic hydrocarbon | Mole ratio ArH: $C_6H_{11}OH$: $AlCl_3$ | Heating regime | | Yield of products (in %) | |
|---|---|---|---|---|---|
| | | temp. | time (in hrs) | mono-substituted | disubstituted |
| o-Xylene | 8.3 : 1 : 0.66 | 65—75° | 4 | 55.8 | — |
| | 8.3 : 1 : 0.82 | 65—75 | 4 | 71.5 | — |
| | 8.3 : 1 : 0.98 | 65—75 | 4 | 71.5 | — |
| m-Xylene | 8.2 : 1 : 0.84 | 65—75 | 4 | 85.9 | — |
| p-Xylene | 8.1 : 1 : 0.80 | 65—75 | 2 | 59.8 | — |
| | 8.1 : 1 : 0.84 | 65—75 | 4 | 68.6 | — |
| Mesitylene | 3.6 : 1 : 0.86 | 60—80 | 4 | 27.2 | — |
| | 5 : 1 : 0.71 | 60—80 | 4 | 35.9 | — |
| Naphthalene | 3.2 : 1 : 0.69 | 45—75 | 4 | 53.3 | 34.2 |
| | 3.2 : 1 : 0.84 | 45—75 | 4 | 58.8 | 39.7 |
| Fluorene | 1 : 1 : 0.85 | 65—100 | 6 | — | — |
| | 1 : 1 : 0.85 | 65—100 | 18 | 32.9 | — |
| | 1.5 : 1 : 0.85 | 65—100 | 50 | 24.2 | — |
| | 0.5 : 1 : 0.85 | 65—100 | 17 | 37.0 | — |

The following products were isolated.

### 4-Cyclohexyl-o-xylene

B. p. 140-142° (17 mm), $n^{20}D$ 1.5271, $d^{20}_4$ 0.9386, $MR_D$ 61.69; calculated 61.05.

Found %: C 88.80; H 10.74. $C_{14}H_{20}$. Calculated %: C 89.29; H 10.71.

Oxidation with dilute (1:4) nitric acid (by long boiling with 15-20 volumes of acid) gave trimellitic acid with m. p. 218° (from water).

### 5-Cyclohexyl-m-xylene

B. p. 138-139° (15 mm), $n^{20}D$ 1.5225, $d^{20}_4$ 0.9343, $MR_D$ 61.52; calculated 61.05. Literature: b. p. 266-268°, $n^{18}D$ 1.5250, $d^{18}_4$ 0.931 [3].

Oxidation with nitric acid gave trimesic acid with m. p. above 300°. Treatment of the acid with diazomethane gave the trimethyl ester with m. p. 140-143° (from alcohol).

### 2-Cyclohexyl-p-xylene

B. p. 138-140° (18 mm), $n^{20}D$ 1.5230, $d^{20}_4$ 0.9348, $MR_D$ 61.53; calculated 61.05. Literature: b. p. 261-262°, $n^{18}D$ 1.529, $d^{18}_4$ 0.9360 [3].

Oxidation gave trimellitic acid with m. p. 218°.

### Cyclohexylmesitylene

B. p. 146-148° (12 mm), $n^{20}D$ 1.5275, $d^{20}_4$ 0.9337, $MR_D$ 66.68; calculated 65.67. Literature: b. p. 283-284.5°, $n^{9}D$ 1.535, $d^{9}_4$ 0.946 [3].

Oxidation with dilute nitric acid gave an acid with m. p. 215-230°.

### β-Cyclohexylnaphthalene

B. p. 162-164° (6 mm), 145-148° (2 mm), $n^{20}D$ 1.5985, $d^{20}_4$ 1.0211, $MR_D$ 70.31; calculated 67.17.

β-Cyclohexylnaphthalene on cooling congealed to a white crystalline mass. The crystals, pressed on porous plate, had m. p. 31°. Literature: b. p. 190-195° (15 mm), 170-180° (3 mm); m. p. 31° [7, 9].

Dehydrogenation of β-cyclohexylnaphthalene with selenium at 300-350° gave β-phenylnaphthalene with m.p. 100° (from alcohol). According to the literature, β-phenylnaphthalene melts at 102° [16].

Dicyclohexylnaphthalene. B. p. 210-220° (5 mm); the main portion distilled at 220°. On long standing the fraction crystallized. The crystals, pressed on porous plate and recrystallized from acetone, melted at 150-151°, which corresponds to 2,6-dicyclohexylnaphthalene [10, 11].

Cyclohexylfluorene. The compound was isolated as the fraction with b. p. 180-190° (5 mm), which immediately crystallized. After several recrystallizations from alcohol the compound was obtained as tiny white crystals with m. p. 133°. Readily soluble in benzene, ether and hot alcohol.

Found %: C 92.24; H 8.56. $C_{19}H_{20}$. Calculated %: C 91.88; H 8.12.

The mixing of benzene solutions of picric acid and cyclohexylfluorene gave a dark-red color, but the picrate underwent decomposition when its isolation was attempted.

## SUMMARY

The condensation of cyclohexanol with the xylenes, mesitylene, naphthalene and fluorene in the presence of aluminum chloride gave the cyclohexyl derivatives of these hydrocarbons.

## LITERATURE CITED

[1] N. G. Sidorova and I. A. Tuchinskaia, J. Gen. Chem. 27, 763 (1957).*

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* Original Russian pagination. See C. B. Translation.

[2] M. Battegay and M. Kappeler, Zbl. II, 2026 (1924).

[3] D. Bodroux, Zbl. I, 2714 (1928).

[4] W. J. Hickinbottom, N. W. Rodgers and N. G. Rule, Abstract Journal, Chemistry, 55031 (1955).

[5] D. Bodroux, Zbl. II, 1531 (1929).

[6] U. S. Patent 1,969,984; Zbl. I, 2258 (1935).

[7] E. S. Pokrovskaia and T. G. Stepantsova, J. Gen. Chem. 9, 1953 (1939).

[8] N. P. Buu-Hoi and P. Cagniant, Ch. A. 41, 5460 (1947).

[9] C. C. Price and J. M. Ciskowski, J. Am. Chem. Soc. 60, 2499 (1938).

[10] C. C. Price, H. M. Shafer, M. F. Huber and C. Bernstein, Ch. A. 37, 1420 (1943).

[11] C. C. Price and A. J. Tomisek, J. Am. Chem. Soc. 65, 439 (1943).

[12] G. Goldschmidt, Monatsh. 2, 433 (1881).

[13] V. N. Ipatieff, H. Pines and V. Komarewsky, Zbl. I, 1138 (1937).

[14] P. Cagniant, A. Deluzarche and M. Colomb, Ch. A. 40, 2286 (1946).

[15] N. A. Shimanko, Dissertation "Study of the Absorption Spectra of Some Polycyclic Hydrocarbons" (1956).*

[16] Chemists Handbook [in Russian] Vol. 2 (Moscow, 1951).

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* In Russian.

# SYNTHESIS OF 1,4-DIISOPROPYLBENZENE AND SOME OF ITS TRANSFORMATIONS

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Dialkylbenzenes are usually formed in the synthesis of monoalkylbenzenes and are regarded as undesirable by-products. It was shown recently that it is possible to convert dialkylbenzenes to phthalic acids and diatomic phenols. Of especial interest here was the synthesis of terephthalic acid and hydroquinone by the oxidation of 1,4-dialkylbenzenes. In connection with this we undertook a broad investigation on the alkylation of monoalkylbenzenes with olefins.

The alkylation of toluene and ethylbenzene with pseudobutylene in the presence of $BF_3 \cdot H_3PO_4$ was described in one of our communications [1], and it was shown that the catalyst $BF_3 \cdot H_3PO_4$ directs the secondary butyl radical mainly in the para-position and makes it possible to obtain 1-methyl-4-sec-butylbenzene and 1-ethyl-4-sec-butylbenzene in yields of 81-84 and 71-73%, respectively.

In this paper we studied the alkylation of isopropylbenzene with propylene in the presence of $BF_3 \cdot H_3PO_4$. It was found that 1,4-diisopropylbenzene is obtained in 73% yield if the isopropylbenzene, propylene and catalyst are taken in the mole ratio 4:1:0.26 and the reaction is run at 98-100°. Under the same conditions, but with the mole ratio of reactants and catalyst taken equal to 3:1:0.2, the yield of 1,4-diisopropylbenzene is 61%, and if run at a temperature of 52-55° the yield drops to 19%.

We studied the liquid-phase oxidation of 1,4-diisopropylbenzene with atmospheric oxygen in the presence of various initiators to the mono- and dihydroperoxides.

As our studies revealed, the oxidation of 1,4-diisopropylbenzene proceeds in such manner that for some time the hydroperoxide accumulates up to a certain maximum, after which the hydroperoxide begins to decompose, and its amount in solution decreases. At 110° such a maximum is reached in 12-14 hours, and at 85° it is reached in 20-40 hours, in both cases depending on the initiator.

The mixed initiator, manganese resinate and cobalt acetate, with calcium hydroxide as the additive, is a more vigorous oxidation initiator at 110° than either the manganese resinate or cobalt acetate taken separately, with the same additive.

The addition of sodium stearate to the mixed initiator of manganese resinate, cobalt acetate and calcium hydroxide accelerates the oxidation and permits obtaining a 51% yield of the hydroperoxide in 17 hours, whereas when the indicated mixture of initiators is used without the addition of sodium stearate the extent of oxidation reaches only 33% at 110° in 16 hours, after which the hydroperoxide begins to decompose. The addition, besides sodium stearate, of small amounts of sodium hydroxide permits oxidizing 1,4-diisopropylbenzene to the hydroperoxide to the extent of 59% in 22 hours.

Calcium hydroxide also accelerates the oxidation and stabilizes the hydroperoxide, thus making it possible to obtain more profound oxidation. Thus, when 1,4-diisopropylbenzene is oxidized in the presence of manganese resinate, cobalt acetate and sodium stearate the extent of oxidation is 33% in 39 hours at 85°. Under the same conditions, but with the addition of calcium hydroxide to the indicated mixture of initiators, the oxidation proceeds to the extent of a 54% yield of hydroperoxide in 24 hours.

The oxidation proceeds mainly toward forming the diisopropylbenzene monohydroperoxide, which when cleaved in acid medium gives 4-isopropylphenol in about 90% yield. A small amount of diisopropylbenzene dihydroperoxide is also formed, which cleaves to hydroquinone.

Cleavage of 1,4-Diisopropylbenzene Hydroperoxide

| Taken for cleavage | | | | | | Amount of cleavage products obtained (in %) | | | |
|---|---|---|---|---|---|---|---|---|---|
| Solution of hydroperoxide in diisopropylbenzene (in g) | Hydroperoxide content (in %) | Calculated as 100% hydroperoxide (in g) | Sulfuric acid (in g) | Acetone (in g) | Cleavage temperature | Acetone | 4-Isopropylphenol | Hydroquinone | Recovered 1,4-diisopropylbenzene |
| 122.7 | 30.7 | 37.7 | 200 (20%) | — | 91° | 47.9 | 32.6 | — | 53.4 |
| 55.2 | 56.6 | 31.2 | 200 (10%) | — | 96-98 | 65.6 | 26.1 | — | 22.1 |
| 43.2 | 39.0 | 16.8 | 200 (7%) | — | 99-100 | 66.9 | 41.0 | — | 25.9 |
| 73.6 | 33.3 | 24.5 | 50 (7%) | — | 98-99 | 74.6 | 67.4 | — | 48.1 |
| 216.5 | 17.2 | 37.2 | 0.5 (conc.) | 5 | 65 | 82.1 | 87.6 | — | 167.1 |
| 62.5 | 83.1 | 53.9 | 150 (conc.) | 85 | 58 | 86.0 | 84.8 | 13.2 | 7.4 |
| 154.8 | 59.0 | 91.3 | 2.8 (conc.) | 2 ml | 100 | 84.6 | 65.6 | 14.6 | 62.1 |

## EXPERIMENTAL

Synthesis of 1,4-diisopropylbenzene. Expt. 1. Into a round-bottomed flask, fitted with stirrer, thermometer and gas-inlet tube, was charged 414 g of $BF_3 \cdot H_3PO_4$ and 3 kg of technical isopropylbenzene with b. p. 149-154°, $d^{20}_4$ 0.8620 and $n^{20}D$ 1.4912. The mixture was heated to 98-100° and then 403 g of propylene (mole ratio of reactants and catalyst 4:1: 0.26) was added at this temperature with vigorous stirring in 3 hours. Then the reaction products were allowed to stand at room temperature for 12 hours, after which the upper hydrocarbon layer was separated from the lower catalyst layer and heated for 1 hour at 100° with calcium hydroxide (7% on weight of alkylate). After such treatment the alkylate was separated from the calcium hydroxide and fractionally distilled through a column with an efficiency of 15-18 theoretical plates.

About 50 g of low-boiling products ($d^{20}_4$ 0.7112, $n^{20}D$ 1.4005) and 2071 g of unreacted isopropylbenzene distilled at atmospheric pressure. The residue was vacuum-distilled. Here we obtained 1130 g (73%) of 1,4-diisopropylbenzene. A residue of 120 g (8%) of polyisopropylbenzenes remained in the distillation flask.

Expt. 2. The reaction of 3 kg of isopropylbenzene, 525 g of propylene and 414 g of $BF_3 \cdot H_3PO_4$ (mole ratio 3:1:0.2) for 3 hours at 98-103° gave 1238 g (61%) of 1,4-diisopropylbenzene and 138 g (7%) of polyisopropylbenzenes. Here 1973 g of unreacted isopropylbenzene was recovered.

Expt. 3. The reaction of 3 kg of isopropylbenzene, 617 g of propylene and 414 g of $BF_3 \cdot H_3PO_4$ (mole ratio 2.75:1:0.17) for 4 hours at 52-55° gave 444 g (19%) of 1,4-diisopropylbenzene and 26 g (1%) of polyisopropylbenzenes. Here 2640 g of unreacted isopropylbenzene was recovered.

1,4-Diisopropylbenzene (distilled twice) is a mobile liquid with a pleasant odor.

B. p. 209-211°, $d^{20}_4$ 0.8570, $n^{20}D$ 1.4898. Literature [2]: b. p. 210.4°, $d^{20}_4$ 0.8568, $n^{20}D$ 1.4898.

2,5-Diisopropylacetanilide. Ten grams of 1,4-diisopropylbenzene was added to a nitrating mixture [10 g of $HNO_3$ (d 1.42) and 15 g of $H_2SO_4$ (d 1.84)] with ice-salt cooling at such a rate that the reaction temperature did not exceed 30°. Then the reaction mixture was heated for 1 hour at 50°, and the nitration products after cooling were separated from the acid layer, neutralized with soda solution, washed with water, dried, and distilled. We obtained 7.3 g (57%) of 2-nitro-1,4-diisopropylbenzene as a light-yellow oily liquid with a bird cherry odor. B. p. 128-130° (1.5-2 mm), $d^{20}_4$ 1.0168, $n^{20}D$ 1.5220.

A mixture of 6.02 g of 2-nitro-1,4-diisopropylbenzene, 15 ml of ethyl alcohol and 0.3 ml of concentrated hydrochloric

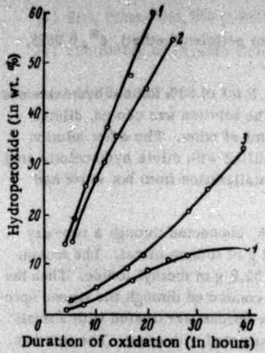

Fig. 1. Oxidation rate of 1,4-diisopropylbenzene at 85°. 1) manganese resinate + calcium hydroxide + sodium stearate + sodium hydroxide; 2) manganese resinate + cobalt acetate + calcium hydroxide + sodium stearate; 3) manganese resinate + cobalt acetate + sodium stearate; 4) sodium stearate.

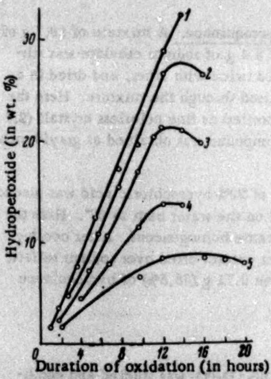

Fig. 2. Oxidation rate of 1,4-diisopropylbenzene at 110°. 1) manganese resinate + cobalt acetate + calcium hydroxide; 2) cobalt acetate + calcium hydroxide; 3) manganese resinate + zinc oxide; 4) manganese resinate + calcium hydroxide; 5) cobalt acetate.

acid was heated to the boil, and after adding 51** g of iron filings in 4 portions, was boiled for 4 hours. Then 0.5 g of solid sodium hydroxide was added, and the 2-amino-1,4-diisopropylbenzene (5.3 g of crude product) was steam-distilled. The amine without purification was mixed with 25 g of 10% acetic acid, and then 3 g of acetic anhydride and one drop of concentrated sulfuric acid were added to the mixture with stirring. The acetanilide, obtained as a white flocculent precipitate, after short standing was filtered and then recrystallized from petroleum ether. It had m. p. 80-80.5°, which corresponds to 2,5-diisopropylacetanilide [3].

Liquid-phase oxidation of 1,4-diisopropylbenzene with atmospheric oxygen. Air was passed at a rate of 12-18 liters/hour through a porous glass plate sealed in the bottom of the vessel into a mixture of 162 g (1 mole) of 1,4-diisopropylbenzene and definite amounts of initiators* at a given temperature. (The reaction mixture gradually assumed a dark-yellow color.)

The amount of hydroperoxide in percent was determined iodometrically at intervals of 2 to 4 hours. The solution of diisopropylbenzene hydroperoxide is a dark-yellow viscous liquid with a sharp ozone odor. 94% of the hydroperoxide has b. p. 120-126° at 1 mm, $d^{20}_4$ 0.9932, $n^{20}D$ 1.5128. According to the literature [4]: diisopropylbenzene monohydroperoxide has $n^{20}D$ 1.5120.

The results of the oxidations run at 85° are plotted in Fig. 1, and those obtained at 110° are plotted in Fig. 2. The maximum concentration of diisopropylbenzene hydroperoxide, obtained in the presence of various initiators, was 59.8%.

The cleavage of 1,4-diisopropylbenzene hydroperoxide to phenol and acetone, using either sulfuric acid or a mixture of sulfuric acid and acetone, was effected in the following manner. A solution of diisopropylbenzene hydroperoxide was placed in a three-necked flask, fitted with stirrer, reflux condenser and thermometer, and then the sulfuric acid was added slowly with vigorous stirring. The degree of cleavage was determined iodometrically. The cleavage products were treated with ammonia, the acetone was evaporated, and the residue was vacuum-distilled. Here the diisopropylbenzene distilled first, and then the 4-isopropylphenol and hydroquinone.

When dilute sulfuric acid was used for the cleavage it was necessary to heat the mixture to 90-100° to start the reaction, and this favored intense tarring of the cleavage products.

The use of large amounts of sulfuric acid also favors tar formation. The reaction proceeds calmly when small amounts of concentrated sulfuric acid and acetone are used for the cleavage, the mixture heats up to 60-100° in a matter of 10-40 minutes, and only small amounts of tarry products are formed. Some of the data on the cleavage of the hydroperoxide under different conditions are given in the Table.

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* Manganese resinate 0.5-5 mg, other initiators 100-500 mg.

** As in original – Publisher's note.

*4-Isopropylphenol* was obtained as white needles with m. p. 59-60° (from petroleum ether), $d^{20}_4$ 0.9898, $n^{20}D$ 1.5228. Literature [5]: m. p. 61°, $d^{20}_4$ 0.990, $n^{20}D$ 1.5228.

*4-Isopropylphenoxyacetic acid.* A mixture of 1 g of 4-isopropylphenol, 5 ml of 33% sodium hydroxide and 1.5 g of chloroacetic acid was heated for 1 hour on the boiling water bath. The solution was cooled, diluted with 10 ml of water, acidified with hydrochloric acid, and extracted with 50 ml of ether. The ether solution was washed with water, shaken with 25 ml of 5% soda solution, and again acidified with dilute hydrochloric acid. The tiny white needles of 4-isopropylphenoxyacetic acid obtained after recrystallization from hot water had m.p. 80°, which agrees with the literature.

*Methyl ether of 4-isopropylphenol.* Into a 100-ml round-bottomed flask, connected through a two-way opening with a reflux condenser, was charged 50 ml of ethyl alcohol and 3.68 g of sodium metal. The sodium ethylate solution was cooled and mixed with 22.6 g of 4-isopropylphenol and 31.5 g of methyl iodide. Then the mixture was heated on the boiling water bath until neutral, and the flask was connected through the second opening to a descending condenser; after removal of the alcohol by distillation the residue was treated with a small amount of water to dissolve sodium iodide, and the 4-isopropylanisole was extracted with ether. The solution was shaken with dilute aqueous sodium hydroxide (to remove 4-isopropylphenol), dried over calcium chloride, and distilled. We obtained 19.98 g (80%) of the ether.

B. p. 95-96° at 19 mm, $d^{17}_4$ 0.9495, $n^{17}D$ 1.5044. Literature [5]: $d^{17}_4$ 0.9495, $n^{17}D$ 1.5045.

The cleavage of 32.6 g of 28% diisopropylbenzene hydroperoxide (9.13 g, calculated as 100% monohydroperoxide) by heating with 40 ml of 30% potassium hydroxide solution at 120° for 1 hour gave 5.87 g (70%) of dimethylcumenylcarbinol with b. p. 94-99° (mainly 97°) at 1.5-2 mm, $d^{20}_4$ 0.9777, $n^{20}D$ 1.5100, $MR_D$ 54.50; calculated 55.54.

*Dimethylcumenylcarbinol* on standing changes into white needle crystals with m. p. 58° (from petroleum ether).

*Isolation of diisopropylbenzene dihydroperoxide and its cleavage to hydroquinone.* A mixture of 19.7 g of 86% diisopropylbenzene hydroperoxide and 30 ml of an alcoholic solution of 5.4 g of sodium ethylate was stirred well with ice-salt cooling. The obtained precipitate was filtered, washed twice with ether, and dried in a vacuum-desiccator. Then it was placed in water and carbon dioxide was passed through the mixture. Here the sodium salt was converted to diisopropylbenzene dihydroperoxide, which deposited as fine colorless crystals (2.6 g). After recrystallization from a mixture of alcohol and petroleum ether the compound was obtained as grayish needles with m. p. 141°, which agrees with the literature [4].

A mixture of 1.86 g of diisopropylbenzene dihydroperoxide and 15 ml of 20% hydrochloric acid was placed in a 50-ml round-bottomed flask, fitted with a reflux condenser, and heated on the water bath to 67°. Here the dihydroperoxide suffered vigorous cleavage, and the mixture frothed and became homogeneous. After cooling to room temperature the cleavage products were treated with ether, the ether extract dried over sodium sulfate, and then separated from the latter by decantation. Removal of the ether gave 0.71 g (78.5%) of hydroquinone with m. p. 168.5° (after recrystallization from water).

## SUMMARY

The alkylation of isopropylbenzene with propylene in the presence of $BF_3 \cdot H_3PO_4$ was studied and conditions were found under which 1,4-diisopropylbenzene is obtained in 73% yield.

Some initiators were found and also the conditions under which 1,4-diisopropylbenzene is oxidized with atmospheric oxygen to give a 59% yield of the hydroperoxide.

## LITERATURE CITED

[1] S. V. Zavgorodnii, T. G. Fedoseeva and A. Ia. Shumakher, Trans. Voronezh State Univ. 57 (1958).

[2] R. D. Obolentsev, Physical Constants of Hydrocarbons of Liquid Fuels and Oils [In Russian] (Gostoptekhizdat, 1953).

[3] Newton, J. Am. Chem. Soc. 65, 2434 (1943).

[4] Brit. Patent 641,250 (1950); C. A. 45, 8042 (1951).

[5] Dictionary of Organic Compounds [Russian translation] Vol. 2, p. 459 (1949).

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# ABSORPTION SPECTRUM OF 1,3-CYCLOHEXADIENE IN THE 220-300 mμ REGION

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The absorption spectrum of 1,3-cyclohexadiene in the ultraviolet region has been investigated in a number of papers [1-3]; however the data of the various authors are not in complete agreement.

The positions of the maxima and the absorption coefficients, found by various authors, are given in Table 1.

TABLE 1

Positions of Absorption Maxima and Values of Molecular Absorption Coefficients for 1,3-Cyclohexadiene Based on the Data of Various Authors

| Authors | Method used to prepare 1,3-cyclohexadiene | State of the compound when taking the absorption spectra | $\lambda_{max}$ (in mμ) | log ε |
|---|---|---|---|---|
| Stark and Levy [1] | From 1,2-dibromocyclohexane | Vapor | 213 | – |
| | | | 260 | – |
| Allsopp [2] | – | Solution in cyclohexane | 256 | 3.98 |
| | | | 267.5 | 3.82 |
| Henri and Pickett [3] | From ethyl-$\Delta^2$-cyclohexenyl ether | Vapor | 251.2 | 3.87 |
| | | | 243.6 | 3.83 |
| | | | 241.4 | 3.86 |
| | | | 234.2 | 3.63 |
| | | | 232.1 | 3.62 |
| | | Solution in hexane | 265.3 | 3.78 |
| | | | 256 | 3.90 |
| | | | 247.5 | 3.73 |

The data given in Table 1 indicate that the results obtained by the different authors in studying the absorption spectrum of 1,3-cyclohexadiene in the ultraviolet region differ among themselves primarily in the number of maxima appearing on the absorption curve. It is possible that the differences in the data of the various authors are due to insufficient purity of the investigated compound. In this connection we investigated the absorption spectrum in the ultraviolet region of a 1,3-cyclohexadiene specimen* that we felt justified in considering to be purer than the specimens available to the other investigators.

## EXPERIMENTAL

Prior to experiment the 1,3-cyclohexadiene was distilled from $MgSO_4$. It had the following physical constants: b. p. 80.5°, $d^{20}_4$ 0.8440, $n^{20}D$ 1.4746. The 1,3-cyclohexadiene specimen reacted with maleic anhydride without leaving a residue. The hexane and ethyl alcohol, used as solvents, were also redistilled before each

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* Prepared in the Industrial Catalysis Laboratory of the Institute of Chemistry of the Academy of Sciences of White Russia SSR.

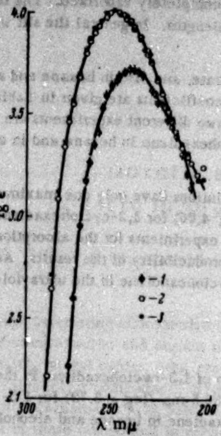

Fig. 1. Molecular absorption coefficient of 1,3-cyclohexadiene vapors (1) and of solutions of 1,3-cyclohexadiene in hexane (2) and in alcohol (3).

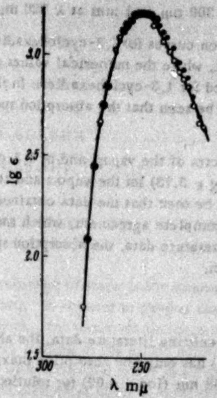

Fig. 2. Reproducibility of the data in measuring the molecular absorption coefficient of 1,3-cyclohexadiene vapors in different experiments.

TABLE 2

Molecular Absorption Coefficients of 1,3-Cyclohexadiene

| Vapors | | Solution in hexane | | Solution in alcohol | | Vapors | | Solution in hexane | | Solution in alcohol | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| (in mμ) | lg ε | (in mμ) | lg ε | (in mμ) | lg ε | (in mμ) | lg ε | (in mμ) | lg ε | (in mμ) | lg ε |
| 220 | 3.15 | 214 | 3.25 | 214 | 3.19 | 252 | 3.72 | 256 | 4.00 | 258 | 4.00 |
| 222 | 3.21 | 217 | 3.21 | 217 | 3.18 | 253 | 3.71 | 258 | 4.01 | 260 | 4.00 |
| 225 | 3.31 | 220 | 3.27 | 220 | 3.17 | 254 | 3.71 | 260 | 4.00 | 262 | 3.99 |
| 228 | 3.40 | 222 | 3.30 | 222 | 3.22 | 256 | 3.69 | 262 | 3.98 | 265 | 3.95 |
| 230 | 3.44 | 225 | 3.34 | 225 | 3.26 | 257 | 3.67 | 264 | 3.96 | 268 | 3.91 |
| 232 | 3.48 | 228 | 3.40 | 228 | 3.32 | 258 | 3.66 | 266 | 3.93 | 270 | 3.86 |
| 235 | 3.55 | 230 | 3.45 | 230 | 3.37 | 259 | 3.64 | 268 | 3.90 | 272 | 3.81 |
| 237 | 3.56 | 232 | 3.52 | 232 | 3.43 | 260 | 3.63 | 270 | 3.86 | 275 | 3.69 |
| 238 | 3.60 | 235 | 3.61 | 235 | 3.61 | 262 | 3.59 | 272 | 3.80 | 278 | 3.56 |
| 240 | 3.62 | 237 | 3.67 | 237 | 3.67 | 264 | 3.53 | 275 | 3.68 | 280 | 3.47 |
| 242 | 3.66 | 240 | 3.76 | 240 | 3.76 | 266 | 3.41 | 278 | 3.55 | 282 | 3.36 |
| 244 | 3.69 | 242 | 3.82 | 242 | 3.80 | 268 | 3.35 | 280 | 3.46 | 285 | 3.12 |
| 246 | 3.71 | 245 | 3.88 | 245 | 3.87 | 270 | 3.26 | 282 | 3.34 | 288 | 2.71 |
| 248 | 3.72 | 248 | 3.93 | 248 | 3.92 | 272 | 3.17 | 285 | 3.08 | 292 | 2.06 |
| 249 | 3.72 | 250 | 3.96 | 250 | 3.95 | 275 | 2.95 | 288 | 2.64 | 295 | 1.53 |
| 250 | 3.72 | 252 | 3.98 | 252 | 3.97 | 278 | 2.59 | 290 | 2.21 | 298 | 1.02 |
| 251 | 3.72 | 254 | 3.99 | 255 | 3.99 | 280 | 2.26 | — | — | — | — |

experiment. They practically failed to absorb light in the ultraviolet region clear up to 215 mμ. An SF-4 spectrophotometer was used to take the absorption spectra. The concentration of 1,3-cyclohexadiene and the thickness of the cuvette were chosen in such manner that the optical density was within the range 0.3-0.9, i.e., in the range where the spectrophotometric measurements are most accurate. To obtain small concentrations of 1,3-cyclohexadiene in the gas phase we introduced a drop of an alcohol solution of 1,3-cyclohexadiene of known weight and concentration into the cuvette, which was then completely vaporized. The slit width selected was the minimum for making measurements at the given wavelengths. In general the slit width changed from 0.2 mm at $\lambda$ 300 mμ to 1 mm at $\lambda$ 220 mμ.

The absorption curves for 1,3-cyclohexadiene in the vapor state, and also in hexane and alcohol solutions, are shown in Fig. 1, while the numerical values of the absorption coefficients are given in Table 2. The absorption curves obtained for 1,3-cyclohexadiene in the vapor state in two different experiments are shown in Fig. 2. From Fig. 1 it can be seen that the absorption spectra of 1,3-cyclohexadiene in hexane and in alcohol coincide completely.

Both the spectra of the vapors and of 1,3-cyclohexadiene solutions have only one maximum, which lies at $\lambda$ 250.5 mμ ($\log \epsilon$ 3.73) for the vapors and at $\lambda$ 258 mμ ($\log \epsilon$ 4.00) for 1,3-cyclohexadiene in solution. From Fig. 2 it can be seen that the data obtained in two different experiments for the absorption spectrum of the vapors are in complete agreement, which indicates a good reproducibility of the results. As a result, contrary to existing literature data, the absorption spectrum of 1,3-cyclohexadiene in the ultraviolet region has only one maximum.

## SUMMARY

Contrary to existing literature data, the absorption spectrum of 1,3-cyclohexadiene in the ultraviolet region (220-300 mμ) has only one absorption maximum, found at 250.5 mμ ($\log \epsilon$ 3.73) for 1,3-cyclohexadiene vapors and at $\lambda$ 258 mμ ($\log \epsilon$ 4.00) for solutions of 1,3-cyclohexadiene in hexane and alcohol.

## LITERATURE CITED

[1] Stark and Levy, Jahrbuch d. Rad. u. Elektronik, 10, 179 (1913).

[2] C. B. Allsopp, Pr. Roy. Soc. 143A, 618 (1934).

[3] V. Henri and L. W. Pickett, J. Chem. Phys. 7, 439 (1939).

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# ISOTOPIC EXCHANGE OF SULFUR IN SALTS OF ORGANIC THIOSULFONIC ACIDS

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One of the most interesting characteristics of the isotopic exchange of sulfur is the unusual rapidity of the reaction between elemental sulfur and certain sulfur-containing salts. In contrast to oxygen compounds of the type of $Na_2CO_3$, $Na_2SO_4$, metal oxides, etc., practically not exchanging (at moderate temperatures) with molecular oxygen, the similar sulfur compounds: $Na_2CS_3$ [1], $Na_2S_2O_3$ [2], sulfides of the alkali metals [3], xanthates ROCSSNa [4] and dithiocarbamates $R_2NCSSNa$ [5], show exchange with elemental sulfur in solutions even in the cold. The behavior of these compounds in exchange reactions with elemental sulfur is quite different from the behavior of other organic sulfur-containing compounds of the type of R–S–R, R–S–S–R, $\begin{matrix}R\\R\end{matrix}\!\!>C{=}S$, etc. In the majority of cases, the exchange proceeds with considerably greater ease in the first group of compounds than in the second.

TABLE 1

| Compound | Formula | Sulfur (in %) | |
|---|---|---|---|
| | | Found | Calculated |
| Sodium ethanethiosulfonate | $C_2H_5SO_2SNa$ | 43.8 | 43.2 |
| Sodium benzenethiosulfonate | $C_6H_5SO_2SNa \cdot 1\frac{1}{2}H_2O$ | 28.8 | 28.6 |
| Sodium p-toluenethiosulfonate | $CH_3C_6H_4SO_2SNa \cdot 2H_2O$ | 26.5 | 26.0 |
| | $CH_3C_6H_4SO_2SNa$ | 30.0 | 30.4 |
| Potassium p-toluenethiosulfonate | $CH_3C_6H_4SO_2SK$ | 27.9 | 28.3 |
| Barium p-toluenethiosulfonate | $(CH_3C_6H_4SO_2S)_2Ba \cdot 5H_2O$ | 20.7 | 21.2 |
| Sodium p-bromobenzenethiosulfonate | $BrC_6H_4SO_2SNa$ | 22.8 | 23.2 |
| Sodium p-nitrobenzenethiosulfonate | $NO_2C_6H_4SO_2SNa$ | 26.0 | 26.5 |
| Sodium p-aminobenzenethiosulfonate | $H_2NC_6H_4SO_2SNa$ | 26.4 | 25.9 |
| Sodium α-naphthalenethiosulfonate | $C_{10}H_7SO_2SNa$ | 26.5 | 26.1 |
| Sodium benzyl thiosulfate | $C_6H_5CH_2S{-}SO_3Na$ | 29.0 | 28.3 |
| Sodium benzenesulfinate | $C_6H_5SO_2Na$ | 20.0 | 19.5 |

In a number of papers it was shown that the exchange reactivity of sulfur in sulfur-containing salts depends to a large degree on the nature of the metal. Exchange proceeds rapidly in the case of the dithiocarbamates and xanthates of sodium [5] and potassium [4], and only slowly at 120-180° in the case of the corresponding lead, zinc, bismuth and nickel salts [6-8]. It was shown [6] on the example of sodium dibutyldithiocarbamate that the rate and energy of activation of exchange with elemental sulfur depend on the polar properties of the solvent. The greater the dissociation capacity of the solvent, the more rapid is the isotopic exchange of sulfur. These facts serve as evidence that ions participate in the exchange reaction with elemental sulfur. One of the principal factors responsible for such a specific behavior of the indicated reactions is apparently the great ease with which the sulfur molecule is polarized by anions.

Our purpose in the present investigation was to make a more detailed study of the basic rules governing the exchange reactivity of sulfur in sulfur-containing salts, and also to elucidate the mechanism of the indicated exchange reactions.

As the object of study we selected a group of compounds that have remained unstudied in this respect up to now, namely the salts of various thiosulfonic acids, depicted by the formula $R{-}SO_2SMe$. Thiosulfonic acid derivatives find wide use in chemical practice as intermediates in the synthesis of dyes, pharmaceuticals, etc. For this reason a study of the mobility of the sulfur in these compounds is of great interest. We hoped to obtain some information on the influence exerted by certain factors, both purely structural – in order to determine the relationship existing between the structure and reactivity of the indicated compounds, as well as external factors like solvent and temperature, on the rate of isotopic exchange. We used the radioactive sulfur isotope $S^{35}$ as the labeled atom.

*Synthesis of purification of compounds used.* The alkali metal salts of the thiosulfonic acids were synthesized by us from the corresponding sulfonyl chlorides $RSO_2Cl$ and sulfides $Me_2S$ by methods given in the literature [9]. The barium salt was obtained by precipitation of the sodium salt with barium chloride solution.

In most cases the compounds were purified by repeated recrystallization from alcohol. According to the literature, some of the salts under these conditions give crystallohydrates. To obtain anhydrous compounds we used anhydrous alcohol for recrystallization.

The compounds were identified by analyzing for sulfur by the Carius method. The analysis results of the investigated salts are given in Table 1.

The solvents used in our study were dried and then distilled, taking the fractions with constants corresponding to those given in the literature.

TABLE 2

| Salt | Activity of original sulfur (impulses/min) | Activity of salt after exchange | Calculated activity of salt in the case of exchange | |
|---|---|---|---|---|
| | | | of one sulfur atom | of two sulfur atoms |
| Sodium p-toluenethiosulfonate | 2630 | 638 | 657 | 876 |
| Potassium p-toluenethiosulfonate | 6142 | 1533 | 1535 | 2047 |
| Sodium ethanethiosulfonate | 1306 | 324 | 326 | 435 |
| Sodium p-bromobenzenethiosulfonate | 1600 | 391 | 400 | 533 |

*Isotopic exchange of sulfur in salts of thiosulfonic acids.* By analogy with the exchange of sulfur in sodium thiosulfate $NaO{-}SO_2SNa$ [10], it could be expected that in the organic thiosulfonates of the alkali metals, $RSO_2SNa$, only the bivalent sulfur atom not linked to the radical R will also be capable of exchange reaction. To verify this we performed some experiments on the exchange of sulfur between salts of thiosulfonic acids with various R radicals, on the one hand, and elemental radioactive sulfur on the other. The experiments were run in 0.1N solutions with the ratio of the components 1 mole of salt : 1 atom of sulfur. In view of the fact that the investigated salts are most easily dissolved in polar solvents, and sulfur most easily in nonpolar solvents, we used a toluene-alcohol mixture (1:1.5 by volume) as the solvent.

The specimens for determining the activity of the components after exchange were prepared as benzidine sulfate precipitates, the elemental sulfur of which and of the salt after isolation were oxidized by the Carius method.

The results of these experiments for the equilibrium state of the system are given in Table 2, where the calculated values of the activity in the case of exchange of one and of two sulfur atoms are also given.

From a comparison of the data in Table 1 it is quite obvious that only one sulfur atom in salts of thiosulfonic acids is capable of exchange reaction, independent of the radical R.

Judging by the behavior of sodium thiosulfate in exchange reactions with elemental sulfur [10], and also taking into consideration the fact that sulfur in various valence states does not show exchange [3], it is possible to conclude that it is the bivalent sulfur atom in organic thiosulfates that exchanges.

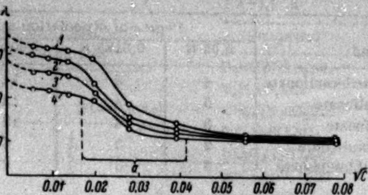

Fig. 1. Conductivity of $NH_2C_6H_4SO_2SNa$ (1), $CH_3C_6H_4SO_2SNa$ (2), $CH_3C_6H_4SO_2SK$ (3) and $NO_2C_6H_4SO_2SNa$ (4) as a function of the concentration.

TABLE 3

Exchange with Elemental Sulfur ($c_{salt} = c_{sulfur} = 0.1$ N in Toluene-Alcohol Mixture)

| Expt. No. | Salt | Formula of substance after exchange | Temperature | $K \cdot 10^4$ | E (kcal/mole) |
|---|---|---|---|---|---|
| 1 | Sodium ethanethiosulfonate | $C_2H_5SO_2S^* Na$ | 45° | 0.279 | 16.6 |
| | | | 57 | 0.703 | |
| | | | 74 | 2.55 | |
| 2 | Sodium benzenethiosulfonate | $C_6H_5SO_2S^* Na$ | 21 | 0.64 | 15.5 |
| | | | 32 | 1.66 | |
| | | | 52 | 8.60 | |
| 3 | Sodium p-bromobenzenethiosulfonate | $BrC_6H_4SO_2S^* Na$ | 21 | 0.195 | 14.7 |
| | | | 41 | 1.0005 | |
| | | | 57 | 3.09 | |
| 4 | Sodium p-nitrobenzenethiosulfonate | $NO_2C_6H_4SO_2S^* Na$ | 41 | 0.988 | 14.8 |
| | | | 50 | 1.92 | |
| | | | 60 | 4.16 | |
| 5 | Sodium p-toluenethiosulfonate | $CH_3C_6H_4SO_2S^* Na \cdot 2H_2O$ | 20 | 0.60 | 14.8 |
| | | | 24 | 0.85 | |
| | | | 30 | 1.01 | |
| | | | 41 | 2.80 | |
| 6 | Sodium α-naphthalenethiosulfonate | $C_{10}H_7SO_2S^* Na$ | 40 | 0.67 | 14.4 |
| | | | 55 | 2.00 | |
| | | | 65 | 4.51 | |
| 7 | Sodium p-aminobenzenethiosulfonate | $H_2NC_6H_4SO_2S^*Na$ | 41 | 3.70 | |
| 8 | Sodium p-toluenethiosulfonate | $CH_3C_6H_4SO_2S^*Na$ | 38.5 | 2.00 | |
| 9 | Potassium p-toluenethiosulfonate | $CH_3C_6H_4SO_2S^*K$ | 38.5 | 0.40 | |
| 10 | Barium p-toluenethiosulfonate | $(CH_3C_6H_4SO_2S^*)_2Ba \cdot 5H_2O$ | 44 (5 hrs) | No exchange | |
| | | | 100 (5 hrs) | | |
| | | | 171 (5 hrs) | | |
| 11 | Sodium benzyl thiosulfate | $C_6H_5CH_2S{-}SO_2{-}ONa$ | 100 (5 hrs) | No exchange | |
| | | | 120 (5 hrs) | | |
| | | | 190 (5 hrs) | | |

TABLE 4

| Compound | Degree of dissociation at 15° (in %) | | | |
|---|---|---|---|---|
| | 0.05 N | 0.0125 N | 0.0031 N | 0.00018 N |
| Sodium p-aminobenzenethiosulfonate | 4 | 6 | 14 | 100 |
| Sodium p-toluenethiosulfonate | 3 | 4 | 12 | 100 |
| Sodium benzenethiosulfonate | 3 | 4 | 12 | 100 |
| Potassium p-toluenethiosulfonate | 2 | 3 | 6 | 100 |
| Sodium p-nitrobenzenethiosulfonate | 3 | 5 | 6 | 80 |

In order to determine the influence exerted by the structure of the radical R and the nature of the metal on the mobility of the sulfur in these compounds, and also to answer some of the questions on the mechanism of the exchange reaction, we quantitatively measured the exchange rate.

The experiments made to measure the kinetics of the exchange of sulfur between a given salt and elemental sulfur were run in toluene-alcohol solvent (1:1.5) and, depending on the experiment temperature, either in a special apparatus [11] or in sealed ampuls in a thermostat. In all of the experiments we took 0.1 N solutions, with the ratio of the components equal to 1 mole of salt : 1 atom of sulfur. The course of the exchange reaction was followed by the change in the activity of the salt. The latter was extracted from the reaction mixture with water, isolated from the solution after evaporation, and purified by recrystallization from water. To determine the activity, the salt precipitates taken were of maximum thickness (190-210 mg per 5 sq cm).

It was established in advance that exchange does not occur with such a method of operation.

We determined the isotopic exchange constants from the equation $K = -\frac{1}{t} \ln \; 1 - \frac{\chi}{\chi_{\infty}}$ expressing the relationship between the activity of the salt $\chi$ and the time $\underline{t}$. The activation energy E was determined for some of the compounds from the values of K as a function of the temperature.

It should be mentioned that the temperature interval was small, only 30 to 40°, and that the accuracy of determining E was of the order 0.5-1 kcal.

The results of measuring the rate with which the sulfur in various salts of thiosulfonic acids exchanges with elemental sulfur are given in Table 3.

To answer the question as to the mechanism of the investigated exchange reactions it was essential to have some information on the dissociation of salts of thiosulfonic acids in a toluene-alcohol mixture.

We used the compensation method to measure the conductivity of a number of salt solutions at 15° and with the concentrations: $C = 0.05$, 0.025, 0.0125, 0.0062, 0.0031, 0.0015, 0.0007, 0.0003 and 0.0001N.

The results of the measurements are shown in Fig. 1, where the values of $\lambda$ are plotted along the ordinate, and the values of $\sqrt{c}$ along the abscissa.

As can be seen, the curves $\lambda - \sqrt{c}$ have approximately the same shape for all of the compounds investigated. A sharp rise is present in the interval of $\sqrt{c}$ values ranging from 0.04 to 0.02 (region $\underline{a}$). A smooth change in the conductivity is observed above and below these values of $\sqrt{c}$ and a linear relationship is maintained between $\lambda$ and $\sqrt{c}$.

Such a shape for the $\lambda - \sqrt{c}$ curves is apparently due to the specific properties of the solvent used.

The degree of dissociation $\alpha = \frac{\lambda}{\lambda_{\infty}} 100$ shown by all of the investigated compounds rises sharply in the interval of solution concentrations ranging from 0.0015 to 0.0003N. Above and below this range of concentrations the degree of dissociation changes but slightly with dilution.

The degrees of dissociation shown by the investigated compounds at various concentrations, with the exception of region $\underline{a}$, are given in Table 4.

**TABLE 5**

Reaction Rate of Sodium Benzensulfinate with Sulfur in 0.1N Alcohol-Toluene Solutions

| Temperature | K · $10^4$ | E (kcal/mole) |
|---|---|---|
| 20° | 0.66 | 15.4 |
| 30 | 1.55 | |
| 37 | 3.04 | |

**TABLE 6**

| Compound | K · $10^4$ |
|---|---|
| $H_2NC_6H_4SO_2SNa$ | 3.7 |
| $C_6H_5SO_2SNa$ | 3.1 |
| $CH_3C_6H_4SO_2SNa$ | 2.8 |
| $BrC_6H_4SO_2SNa$ | 1.0 |
| $NO_2C_6H_4SO_2SNa$ | 1.0 |
| $\alpha$-$C_{10}H_7SO_2SNa$ | 0.8 |
| $C_2H_5SO_2SNa$ | 0.3 |

## DISCUSSION OF RESULTS

As can be seen from the above material, 1 sulfur atom in the alkali metal salts of organic thiosulfonic acids is exceedingly labile and exchanges with elemental sulfur in 0.1N solutions at 20-40°. Such an atom is the bivalent peripheral sulfur atom in $R-SO_2-S^*Na$.

From a comparison of the data on the exchange reactivity of the sulfur in salts of various metals, sodium, potassium and barium (Table 3, Nos. 8-10), it is obvious that the nature of the metal exerts a very large influence on the mobility of the sulfur atom found in salts of thiosulfonic acids. With other conditions constant, the rate of sulfur exchange in potassium toluenethiosulfonate is 1/6 as fast as in the case of the corresponding sodium compound, while the barium derivative does not exchange with sulfur even at 170°. In this respect the behavior of the thiosulfonate derivatives is similar to that shown by dithiocarbamate [5, 6] and xanthate [4] compounds, where a large difference is also observed in the exchange-reactivity of sulfur as a function of the nature of the metal. What is the reason for such a marked difference in the behavior of the investigated compounds?

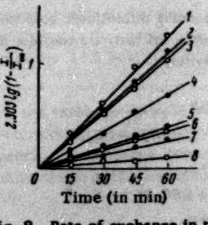

Fig. 2. Rate of exchange in the salts: $NH_2C_6H_4SO_2SNa$ (1), $C_6H_5SO_2SNa$ (2), $CH_3C_6H_4SO_2SNa$ (3), $(CH_3CO)_2NC_6H_4SO_2SNa$ (4), $BrC_6H_4SO_2SNa$ (5), $NO_2C_6H_4SO_2SNa$ (6), $C_{10}H_7SO_2SNa$ (7) and $C_2H_5SO_2SNa$ (8).

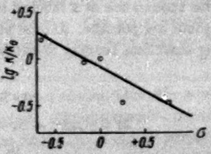

Fig. 3. Relationship between exchange velocity constants and Hammett values σ.

In discussing the exchange reactions of sulfur in the indicated salts, it is important to know the state of the elementary particles entering into exchange reaction with sulfur, i. e., whether they are salt molecules or ions.

On the basis of a number of facts and primarily on the basis of the data in [6] on the rate of sulfur exchange in sodium dibutyldithiocarbamate, which depends on the dissociation ability of the solvent (various mixtures of toluene + alcohol + water), it is possible to conclude that the principal factor, responsible for the rapid exchange shown by the above salt, is the presence of a suitable anion in solution, capable of exchange.

As regards the salts of thiosulfonic acids, it is also most probable to assume that exchange occurs with the participation of ions. If such is true, then a definite relationship should exist between the exchange capacity shown by the compounds and their degree of dissociation.

From a comparison of the data in Table 3, and also in Fig. 1, for the toluenethiosulfonates of sodium, potassium and barium it is quite obvious that both the exchange capacity and the degree of dissociation shown by these compounds changes in the order sodium > potassium ≫ barium.

Potassium toluenethiosulfonate is less dissociated in solution than is the corresponding sodium compound, and exchanges much more slowly. Solutions of barium toluenethiosulfonate are practically nonconductive; the compound does not dissociate into ions and does not exchange.

We found that the addition of a small amount of the sodium salt catalyzes the isotopic exchange of sulfur in the barium derivative. Thus, when the reaction between $(CH_3C_6H_4SO_2S)_2Ba$ and elemental sulfur $S^{35}$ was run in the presence of $CH_3C_6H_4SO_2SNa$ (3% on the weight of barium salt) it was established that the exchange proceeds quite rapidly even at 43°.

In essence it is possible for two independent reactions to proceed in such a system – the exchange of sulfur between sodium toluenethiosulfonate and elemental sulfur and the exchange of $CH_3C_6H_4SO_2S$ groups between the sodium and barium salts.

$$CH_3C_6H_4SO_2S^- + S^* \rightleftarrows CH_3C_6H_4SO_2S^{*-} + S$$

$$CH_3C_6H_4SO_2S{-}Ba{-}SSO_2C_6H_4CH_3 + 2CH_3C_6H_4SO_2S^{*-} \rightleftarrows$$

$$\rightleftarrows CH_3C_6H_4SO_2S^*{-}Ba{-}S^*SO_2C_6H_4CH_3 + CH_3C_6H_4SO_2S^-$$

As a result of these two fairly rapid reactions a labeled sulfur atom appears in the barium salt. The accelerating effect of the sodium derivative reduces to a transfer of labeled $CH_3C_6H_4SO_2S^{*-}$ groups to the barium salt.

A similar mechanism for the catalytic action of the corresponding sodium derivative was convincingly demonstrated [6] in the case of the isotopic exchange of sulfur in nickel diethyldithiocarbamate and in thiuram.

As a result, the specific influence exerted by the nature of the metal (sodium, potassium, barium) on the ability of salts of thiosulfonic acids to exchange is manifested mainly through a variable ability of the corresponding compounds to dissociate into ions.

How can the appearance of a labeled sulfur atom in the corresponding thiosulfonic acid salt be depicted? Here several methods are possible. On the basis of a number of experimental facts we consider it most probable that the following reactions, leading to exchange, are present in the system:

$$1)\ RSO_2SNa \rightleftarrows RSO_2S^- + Na^+$$

$$2)\ RSO_2S^- + S_n \rightarrow RSO_2{-}S{-}S{-}S\ldots S^- \rightleftarrows RSO_2^- + S_{n+1}$$

$$3)\ RSO_2^- + Na^+ \rightleftarrows RSO_2Na$$

$$4)\ RSO_2^- + S^*_n \rightleftarrows RSO_2{-}S^*{-}S^*{-}S^*\ldots S^* \rightarrow RSO_2S^{*-} + S^*_{n-1}$$

$$5)\ RSO_2S^{*-} + Na^+ \rightleftarrows RSO_2S^*Na$$

The given scheme includes the formation of the sodium sulfinate as an intermediate product (2, 3), which then adds the labeled sulfur atom (4, 5).

To obtain proof for such a mechanism we attempted to study the individual stages of this reaction separately and evaluate the energy factors.

As regards the first stage, then here the dissociation of the investigated compounds into ions in the solvent used was shown by us experimentally; in this connection the values given in Table 4 refer to the conductivities of the solutions at 15°, and the salts show a much higher degree of dissociation at the temperatures at which the exchange experiments were run (20-70°).

The fact that sulfinic acid salts are formed (stages 2 and 3) in the reaction of thiosulfonic acid salts with sodium polysulfide and with sodium sulfite has been discussed in the literature [12]. The fact that a sodium sulfinate is formed was confirmed by us by reacting labeled sodium toluenethiosulfonate with sodium sulfite in aqueous solution at 43°.

$$CH_3C_6H_4SO_2S^*Na + Na_2SO_3 \rightarrow CH_3C_6H_4SO_2Na + Na_2S^*SO_3$$

The products isolated from this reaction were sodium toluenesulfinate (with a sulfur content of 17.3% after recrystallization from alcohol; calculated 17.9%), which did not contain any labeled sulfur atoms, and labeled sodium thiosulfate.

The reaction of a sodium sulfinate with elemental sulfur (stages 4 and 5) was studied by us on the example of reacting sodium benzenesulfinate with radioactive sulfur.

The kinetics of the reaction $C_6H_5SO_2Na + S^* \rightarrow C_6H_5SO_2S^*Na$ in toluene-alcohol medium (1:1.5) was measured by us at various temperatures.

The formation rate of the sodium benzenethiosulfonate was determined by quantitative analysis of the product obtained from the reaction mixture. The product was extracted from the reaction mixture with water, and then isolated from the solution after evaporation.

The results are summarized in Table 5.

Quite noteworthy is the fact that the velocity constants for the exchange of sulfur in sodium benzenethiosulfonate at the given temperatures (Table 3, No. 2) are close in value to the velocity constants for the addition of sulfur to sodium benzenesulfinate (Table 5). The energy of activation is the same for both reactions: 15.4 and 15.5 kcal/mole.

We believe that the presented material is quite adequate to justify the conclusion that the above proposed mechanism for the exchange of sulfur in salts of organic thiosulfonic acids is valid.

It should be mentioned that in principle this reaction scheme is analogous to the extensively studied [13] reaction for the exchange of sulfur between sodium thiosulfate and labeled sodium sulfite

$$S_2O_3^= + S^*O_3^= \rightleftarrows SO_3^= + SS^*O_3^=$$

The difference consists in that in the first case the sulfur atom is transferred from the thiosulfonate ion to the sulfur molecule, and in the second case it is transferred to the sulfite ion. The activation energies for the two reactions are close: 14.5 kcal [13] for the thiosulfate-sulfite exchange, and 14-16 kcal for the compounds studied by us.

Apparently, the exchange between elemental sulfur and alkali metal polysulfides also proceeds by a similar scheme of successive acts of transfer and addition of the sulfur atom. The difference consists in that in the polysulfides, together with exchange, there is sulfur addition with the formation of higher polysulfides, while in the case of the thiosulfonic acid salts such addition is not observed, probably due to the instability of such polysulfide compounds.

The sulfur molecule $S_8$ becomes reactive in the presence of suitable sulfur-containing anions in solution, and easily adds sulfur atoms. The principal reason for sulfur behaving in this manner is probably due to the polarizing action exerted by the anion on the sulfur molecule, leading to rupture of the ring.

From the data in Table 3 it can be seen that the exchange capacity shown by thiosulfonic acid salts is influenced not only by the nature of the metal atom, directly attached to the exchanging sulfur atom, but also by the composition and structure of the radical R. The energy of activation for exchange in the investigated compounds is small, and the influence exerted by the radical is manifested very poorly here.

However, this influence is quite distinctly manifested when the exchange rates are compared.

The velocity constants for exchange with an aliphatic radical (ethyl) are approximately 10 times smaller than the velocity constants for exchange with an aromatic radical like phenyl or tolyl.

For greater clarity we have plotted in Fig. 2 the values of $-\ln(1 - x/x_\infty)$ as a function of time, obtained for various compounds in solutions of constant concentration at 41°. The K values corresponding to these data are given in Table 6.

The influence exerted by the radical on the ability of the sulfur in thiosulfonic acid salts to exchange can be manifested to varying degree in the different factors that determine the course of the reactions: stereochemistry of the reactions, degree of dissociation of the corresponding salts, magnitude of the effective charge on the exchanging sulfur atom in the anion of the thiosulfonic acid, etc.

In those cases where the radicals are quite different from each other, for example ethyl and naphthyl, the extent to which each of these factors is manifested can be different, and in order to establish any rules it is necessary to accumulate a much greater amount of experimental data than was obtained in the present study.

In the case where the radicals are close in composition and structure, for example substituted phenyls, the influence exerted on the ability to exchange is more uniform, and a comparison of the data for this type of compound is quite in order. From the data in Table 3 (and also Table 6) on the exchange of sulfur in various substituted sodium benzenethiosulfonate derivatives it can be seen that the introduction of electron-donor substituents ($NH_2$) in the para-position of the benzene ring facilitates exchange, while the introduction of electron-acceptor substituents ($NO_2$, Br) hinders exchange.

The principal factor responsible for the varying ability shown by the sulfur in this series of compounds to exchange is apparently the magnitude of the effective charge on the sulfur atom in the anion of the thiosulfonic acid. The larger the charge, the greater is the polarizing action on the sulfur molecule, and consequently the more probable is the formation of the complex. Electron-acceptor substituents reduce the magnitude of the effective charge, while electron-donor substituents increase it.

As a result, the reactions for the exchange of sulfur between thiosulfonic acid salts and elemental sulfur are heterolytic in nature.

As is known, the influence of substituents on the rate of such reactions obeys the Hammett rule.

We compared the values obtained by us for log $(K/K_0)$, where K is the velocity constant for sulfur exchange in the substituted compound, and for exchange in the unsubstituted compound, with the Hammett values $\sigma$. The results are shown in Fig. 3. As can be seen, within the limits of experimental error, a linear relationship exists between log $(K/K_0)$ and $\sigma$, with $\rho$ equal to $-0.56$.

## SUMMARY

1. The exchange of sulfur between various thiosulfonic acid salts $RSO_2SMe$ and elemental sulfur $S^{35}$ in toluene-alcohol solution was studied at various temperatures. The energy of activation of the exchange reactions was determined.

2. It was shown that both the radical and the metal exert considerable influence on the ability shown by the salts to exchange.

An analysis was given of the influence exerted by the composition and structure of the radicals on exchange.

3. The conductivity of a number of thiosulfonic acid salts in a toluene-alcohol mixture was measured at various salt concentrations. The degree of dissociation was determined.

4. A mechanism for the reaction of sulfur exchange in thiosulfonic acid salts was evolved.

## LITERATURE CITED

[1] R. Edwards, F. Nesbett and A. Solomon, J. Am. Chem. Soc. 70, 1670 (1948).

[2] R. Muxart, B. Boscardin, P. Daudel and P. Wenger, J. Chim. Phys. 47, 606 (1950).

[3] H. Voge and W. F. Libby, J. Am. Chem. Soc. 59, 2474 (1937); E. N. Gur'ianova, Ia. K. Syrkin and L. S. Kuzina, Proc. Acad. Sci. USSR 86, 107 (1952); M. M. Haissinsky and D. Peschanski, J. Chim. Phys. 47, 191 (1950)

[4] M. N. Foka and L. E. Burkser, Proc. Acad. Sci. USSR 99, 1011 (1954).

[5] I. I. Kukhtenko, G. A. Blokh and G. P. Miklukhin, Ukrain. Chem. J. 21, 227 (1955); E. N. Gur'ianova, J. Phys. Chem. (USSR) 28, 70 (1954); I. I. Kukhtenko and G. P. Miklukhin, Proc. Acad. Sci. USSR 100, 931 (1955).

[6] L. S. Kuzina, Dissertation "Isotopic Exchange of Sulfur in Some Derivatives of Dithiocarbamic Acids and Their Structure" (1956).*

[7] G. P. Miklukhin, Supplement "Session of the Academy of Sciences of the USSR on the World-Wide Utilization of Atomic Energy," p. 251 (1955).*

[8] E. N. Gur'ianova, V. N. Vasil'eva and L. S. Kuzina, Supplement "Session of the Academy of Sciences of the USSR on the World-Wide Utilization of Atomic Energy," p. 270 (1955).*

[9] Spring, Ber. 7, 1162 (1874); Otto and Rossing, Ber. 24, 1153 (1891).

[10] E. Andersen, Z. phys. Ch. B 32, 237 (1936); H. Voge, J. Am. Chem. Soc. 61, 1032 (1939); R. Appel, Naturw. 40, 509 (1953).

[11] E. N. Gur'ianova and V. N. Vasil'eva, J. Phys. Chem. (USSR) 29, 576 (1955).

[12] I. L. Khmel'nitskaia and F. M. Kogan, J. Appl. Chem. 25, 1004 (1952).**

[13] D. P. Ames, J. E. Willard, J. Am. Chem. Soc. 73, 164 (1951).

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# SYNTHESIS OF UNSYMMETRICAL DIALKYLHYDRAZINES

## B. V. Ioffe

The most convenient method for the synthesis of unsymmetrical secondary hydrazines is the reduction of nitrosamines with a large excess of zinc dust in acetic acid medium [1-4]. Only the method for the preparation of dimethylhydrazine [4] has been developed in detail, but this same method has also been used to obtain both diethylhydrazine [1, 2] and (in somewhat lower yields) the simpler aromatic hydrazines [3]. An attempt [5] to synthesize mixed unsymmetrical aliphatic hydrazines (methylpropyl-, methylisobutyl- and methylisoamylhydrazines) by this method proved unsuccessful: reduction of the nitrosamines gave the corresponding secondary amines, and only once, when the reaction with methylisobutylnitrosamine was run in the cold did it prove possible to isolate a small amount of methylisobutylhydrazine as the methyl isobutylsemicarbazide. Unsatisfactory results were also obtained when this method was used to synthesize the dipropyl- and dibutylhydrazines [6], and reduction of the nitrosamines with aluminum lithium hydride has been recommended as a method for the preparation of these compounds [6, 7].

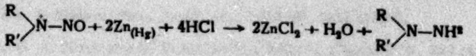
TABLE 1

Yields of Secondary Amines and Hydrazines in the Reduction of Nitrosamine with Zinc Amalgam in Hydrochloric Acid Medium

| Nitrosamine | Yield (in mole %) | |
|---|---|---|
| | secondary amine | secondary hydrazine |
| Diethylnitrosamine | 12 | 69 |
| Methyl-n-propylnitrosamine | 8 | 71 |
| Methylisopropylnitrosamine | 10 | 59 |
| Methyl-n-butylnitrosamine | 16 | 69 |
| Methylisobutylnitrosamine | 16 | 76 |
| Di-n-propylnitrosamine | 21 | 70 |
| Di-n-butylnitrosamine | 30 | 48 |
| Methylphenylnitrosamine | 71 | 0 |

Reduction with sodium in alcohol and with sodium in liquid ammonia in the presence of alcohol have also been proposed recently as methods for the preparation of hydrazines from nitrosamines [7].

In this communication we propose a method for the synthesis of unsymmetrical dialkylhydrazines, differing from previously described methods in its simplicity, lower consumption of reagents, and good yields of hydrazines. The method recommended by us is based on the reduction of nitrosamines with zinc amalgam in hydrochloric acid medium.



$$\begin{matrix}R\\R'\end{matrix}\!\!>\!N{-}NO + 2Zn_{(Hg)} + 4HCl \longrightarrow 2ZnCl_2 + H_2O + \begin{matrix}R\\R'\end{matrix}\!\!>\!N{-}NH^{2} \qquad (1)$$

TABLE 2

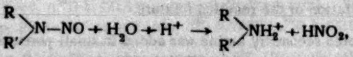
Unsymmetrical Secondary Hydrazines, Obtained by the Reduction of Nitrosamines with Zinc Amalgam

| Unsymmetrical hydrazines | Boiling point (pressure in mm) | $d^{20}_4$ | $n^{20}D$ | $MR_D$ | |
|---|---|---|---|---|---|
| | | | | Found | Calculated[*] |
| Diethylhydrazine | 98.0- 99.6° (756) | 0.8004 | 1.4214 | 27.95 | 28.00 |
| Methyl-n-propylhydrazine | 103.2-103.7 (753) | 0.7986 | 1.4208 | 27.98 | 28.00 |
| Methylisopropylhydrazine | 101.3-101.7 (769) | 0.8096 | 1.4234 | 27.75 | 28.00 |
| Methyl-n-butylhydrazine | 128.0-128.2 (736) | 0.8028 | 1.4267 | 32.66 | 32.65 |
| Methylisobutylhydrazine | 115.4-115.9 (758) | 0.7930 | 1.4207 | 32.65 | 32.65 |
| Di-n-propylhydrazine | 141.0-142.2 (764) | 0.8008 | 1.4270 | 37.26 | 37.30 |
| Di-n-butylhydrazine | 79.5- 81 (20) | 0.8089 | 1.4347 | 46.51 | 46.59 |

The reduction is run by simply shaking the nitrosamine with dilute hydrochloric acid (1:1) and granulated zinc, covered with mercury. Due to the high hydrogen overvoltage on pure zinc amalgam the evolution of hydrogen fails to occur, and the reduction proceeds so rapidly and vigorously that it is necessary to cool the reaction mixture by the addition of ice.

The use of amalgam makes it possible to run the reaction in an ordinary separatory funnel and reduce the zinc consumption to the stoichiometric amount, i.e., to reduce the amount consumed to nearly 1/10 of that required with the Fischer method [1-4].

A secondary reaction in our method is the hydrolytic cleavage of the nitrosamines to secondary amine salts and nitrous acid



$$RR'N{-}NO + H_2O + H^+ \rightarrow RR'NH_2^+ + HNO_2, \qquad (2)$$

which is then reduced further to ammonia [1, 2], nitric oxide and, possibly, in part to nitrous oxide.

The ratio of the yields of main and secondary products (hydrazines and amines) depends on the nature of the nitrosamines and the reaction conditions. Quantitative data on the yields of amines as secondary products of the reduction of nitrosamines have been nonexistent up to now. The analysis results obtained for the mixtures of bases, formed under the conditions recommended by us, are given in Table 1. As can be seen from these results, the role of the secondary reaction (2) increases with increase in the length of the hydrocarbon radicals. However, the yields of the dialkylhydrazines up to dibutylhydrazine remain excellent.

In attempting to use the described method to obtain the simplest aryl alky hydrazine, unsym.-methylphenylhydrazine, it was found that the nitroso group is eliminated completely and the product obtained is pure N-methylaniline. Evidently, due to the great ease with which aromatic nitrosamines are hydrolyzed, the recommended method is not suitable for the synthesis of hydrazines with aromatic radicals.

The homologs of unsym.-dimethylhydrazine have been studied but slightly up to now.

The seven unsymmetrical aliphatic hydrazines synthesized in this paper were characterized by determining their physical constants (see Table 2), in which connection three of them are new (methyl-n-propyl-, methylisopropyl- and methylisobutylhydrazine). The new homologs of unsym.-dimethylhydrazine are colorless liquids with a characteristic odor, differing from the odor of amines, readily soluble in water and, using methyl orange as indicator, titrate as monoacidic bases in aqueous solution.

## EXPERIMENTAL[**]

Synthesis of nitrosamines. Dimethylnitrosamine was obtained by the distillation of a mixture of concentrated

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[*] Using the bond refractions of Vogel (see [6] and [11], p. 182).

[**] Student L. E. Poroshina assisted in the work.

TABLE 3

Properties of Nitrosamines Used for the Synthesis of Unsymmetrical Secondary Hydrazines

| Nitrosamines | Boiling point at 40 mm | $d^{20}_4$ | $n^{20}D$ |
|---|---|---|---|
| Dimethylnitrosamine | 67.1-67.2° | 1.0048 | 1.4368 |
| Diethylnitrosamine | 86.7-86.8 | 0.9424 | 1.4386 |
| Di-n-propylnitrosamine | 113.2 | 0.9153 | 1.4440 |
| Di-n-butylnitrosamine | 118-118.3 (15 mm) | 0.8997 | 1.4478 |
| Methyl-n-propylnitrosamine | 90.4-91.2 | 0.9454 | 1.4414 |
| Methylisopropylnitrosamine | 87.6-87.9 | 0.9452 | 1.4402 |
| Methyl-n-butylnitrosamine | 107.1-107.7 | 0.9298 | 1.4443 |
| Methylisobutylnitrosamine | 99.7 | 0.9244 | 1.4420 |
| Methylphenylnitrosamine | 132-134 (22 mm) | 1.1282 | 1.5777 |

dimethylamine hydrochloride and sodium nitrite (taken in slight excess) solutions, followed by salting out of the distillate with potash [8]. To remove amine impurities the salted out organic layer was shaken for a short time with potassium bisulfate, then dried over potash, and distilled through a column (12 theoretical plates). The yield of product, with the constants given in Table 3, was 76%.

Diethylnitrosamine was obtained in a similar manner in 74% yield.

For the difficultly water-soluble nitrosamines with larger radicals it is expedient to use the method described below, not requiring distillation of the reaction mixture.

One gram-mole of ice-cooled secondary amine was added in small portions with stirring to a cooled mixture of 87 ml of concentrated hydrochloric acid (d 1.18) and 115 ml of water. To the obtained solution was added 76 g (1.1 g-mole) of sodium nitrite and the mixture was boiled under reflux for 40-60 minutes. The yellow layer of nitrosamine was separated, dried over potash, and fractionated through a column at 40 mm. The yields of pure nitrosamines by this method ranged from 87 to 91%.

Methylphenylnitrosamine was synthesized from technical methylaniline by the method of Hartman and Roll [9].

Reduction of nitrosamines with zinc amalgam. Into a 2.5-liter separatory funnel was placed 132 g (2.02 g-atom) of granulated zinc (arsenic-free) and 15 ml of mercury. Then 0.5 kg of ice was added, after which 450 ml of concentrated hydrochloric acid (d 1.18) was added gradually, with slight shaking of the funnel so that the surface of the zinc remained covered by the mercury and hydrogen was not evolved. Then 1 g-mole of the nitrosamine was added in portions. Approximately one third of the total nitrosamine was added at the start and the mixture shaken vigorously until heat was no longer evolved. The remaining nitrosamine was added in several portions, at the same time adding ice (another 0.5 kg in portions) to the reaction mixture. After each addition of nitrosamine and ice the mixture was shaken vigorously until reaction ceased. The amounts of nitrosamine added, the addition of ice, and the vigor of shaking, were regulated in such manner that the temperature in the funnel did not rise too high (up to 60°) and the funnel could be handled manually.

When all of the nitrosamine had been added the vigorous shaking was continued until heat was no longer evolved, the odor of the nitrosamine had disappeared, and nearly all of the zinc granules had dissolved.

The total time required to run the reaction with the indicated amounts of reactants is about 3/4 hour. The mercury layer is separated and can be used in subsequent experiments. The water layer is mixed with 300 ml of 50% sodium hydroxide solution in a three-liter round-bottomed flask. The flask is then connected through a spray catcher to a descending condenser and the volatile bases are steam-distilled.

The optimum amounts of distillate and alkali for salting out are indicated below for each compound.

The organic bases, salted out from the distillate with sodium hydroxide, after drying over solid caustic were distilled through a Vigreux column with a rated efficiency of 15 theoretical plates. The receivers were protected from atmospheric moisture and carbon dioxide by a soda lime tube.

The first fractions represent secondary reduction products – the secondary amines, and the last fractions represent the hydrazines. Small amounts of water, usually present despite the drying over caustic, distill either as minimum azeotropes with the amines, provided the boiling points of the latter are close to 100°, or with the hydrazines. In the latter case the pure hydrazine fraction precedes the water-containing hydrazine fraction, having higher density and refractive index values.

The yields of amines and hydrazines given in Table 1 were calculated from the analysis data obtained in the titration of the fractions and residue with 0.1N hydrochloric acid, using methyl orange as indicator. Small intermediate fractions were considered to be binary mixtures of amine and hydrazine and were analyzed by refractive index.

Unsym.-diethylhydrazine. After the reduction of 102 g of diethylnitrosamine under the above described conditions we took 300 ml of the aqueous distillate and added 120 g of sodium hydroxide to it with cooling. The separated layer of 78.4 g of organic bases was dried over solid sodium hydroxide and then distilled through the column at 756 mm. The following fractions were obtained:

1st, 52-57.5°, 8.2 g, $d^{20}_4$ 0.7074, $n^{20}$D 1.3848 (diethylamine).

Pure diethylamine, according to our data, has b. p. 56.1-56.2° at 776 mm, $d^{20}_4$ 0.7053, $n^{20}$D 1.3850.

2nd, 57.5-88°, 1.3 g, $n^{20}$D 1.4006 – mixture of amine and hydrazine (with a small amount of water). Amount of amine, based on $n^{20}$D, 58%.

3rd, 88-98°, 6.2 g, $n^{20}$D 1.4224 – diethylhydrazine with water as impurity. Diethylhydrazine content 88.3%.

4th, 98-99.6°, 53 g, $d^{20}_4$ 0.8004, $n^{20}$D 1.4214 – unsym.-diethylhydrazine. Yield 60.2%. Literature for unsym diethylhydrazine [6]: b. p. 99.5-100° at 762 mm, $d^{20}_4$ 0.7988, $n^{20}$D 1.42136.

Residue, 6.4 g, $n^{20}$D 1.4330. Diethylhydrazine content 41.9%. Partially soluble in water. The water-insoluble yellow layer after washing and drying over potash had $n^{20}$D 1.4443 (diethylnitrosamine).

Unsym.-di-n-propylhydrazine. For reduction we took 97.7 g (0.75 g-mole) of di-n-propylnitrosamine and correspondingly smaller amounts of the other reactants. For salting out 200 ml of distillate we used 70 g of sodium hydroxide. The salted out organic layer after drying was fractionally distilled to give 53.2 g (61%) of di-n-propylhydrazine:

B. p. 141.0-142.2° (at 764 mm), $d^{20}_4$ 0.8008, $n^{20}$D 1.4270. Literature [6]: b. p. 140.5-141° (768 mm), 31.5° (7 mm), $d^{20}_4$ 0.7997, $n^{20}$D 1.42661.

When an acetic acid solution of the dipropylhydrazine was heated with concentrated potassium cyanate solution we obtained 1,1-di-n-propylsemicarbazide, which after recrystallization from dilute alcohol (1:1) had m. p. 114-115°. Literature [7]: m. p. 116°.

The intermediate fraction with b. p. 111-141° and the distillation residue contained (based on the analysis data) another 7.4 g of the di-n-propylhydrazine.

As a secondary product of the reduction we obtained 9.7 g (12.8%) of di-n-propylamine: b. p. 108-111° (764 mm), $d^{20}_4$ 0.7414, $n^{20}$D 1.4052.

Pure di-n-propylamine has, according to our data, b. p. 108.7-108.9° (751 mm), $d^{20}_4$ 0.7378, $n^{20}$D 1.4042.

Another 6.2 g of di-n-propylamine was contained in the first (up to 108°) and intermediate (111-141°) fractions.

Unsym.-di-n-butylhydrazine. In the reduction of 62.6 g (0.4 g-mole) of di-n-butylnitrosamine we observed a weaker evolution of heat than in the case of the nitrosamines with smaller radicals, and here 15 g of unreacted zinc remained. The reaction mixture at the end of reduction was still heterogeneous; the organic layer congealed to a crystalline mass.

We removed 200 ml of the heterogeneous distillate. The water layer was salted out with 80 g of sodium hydroxide. After drying over solid caustic the organic layer was distilled through the column at 20 mm: 1st fraction with b. p. 58.5-62° (11.1 g) was di-n-butylamine ($d^{20}_4$ 0.7626, $n^{20}D$ 1.4182); 2nd fraction with b. p. 62-72.5° (7.7 g) was an intermediate fraction ($n^{20}D$ 1.4264); 3rd fraction (21.4 g, 37.4%) was pure di-n-butylhydrazine:

B. p. 79.5-81° (20 mm), $d^{20}_4$ 0.8089, $n^{20}D$ 1.4347.

Found: equiv. weight 143.4, 144.7. $(C_4H_9)_2N_2H_2$. Calculated: equiv. weight 144.3.

Literature [6]: B. p. 61° (8 mm), $d^{20}_4$ 0.8078, $n^{20}D$ 1.43430.

The 1,1-di-n-butylsemicarbazide obtained from the 3rd fraction had m. p. 92° (from 50% alcohol). Literature [7]: m. p. 94°.

The distillation residue (5.3 g) contained another 2.4 g of di-n-butylhydrazine.

Unsym-methyl-n-propylhydrazine. After the reduction of 45.9 g (0.45 g-mole) of methyl-n-propylnitrosamine we removed 250 ml of alkaline distillate, which was saturated with sodium hydroxide (110 g). We obtained 7.3 g of wet 96.5% methyl-n-propylhydrazine (b. p. 96.7-103.2°, $d^{20}_4$ 0.8044, $n^{20}D$ 1.4214) and 15.9 g (40.1%) of pure methyl-n-propylhydrazine with the following constants:

B. p. 103.2-103.7° (753 mm), $d^{20}_4$ 0.7986, $n^{20}D$ 1.4208.

Found: equiv. weight 88.7, 89.7. $C_4H_{10}N_2H_2$. Calculated: equiv. weight 88.15.

Methyl-n-propylhydrazine is not described in the literature.

The distillation residue (4.5 g) and intermediate fraction with b. p. 63-96.7° (1.8 g, $n^{20}D$ 1.4120) contained another 5.3 g of methylpropylhydrazine.

The first fraction (2.1 g) was methyl-n-propylamine:

B. p. 60.3-63° (753 mm), $d^{20}_4$ 0.7179, $n^{20}D$ 1.3907.

Found: equiv. weight 74.2, 74.3. $C_4H_{11}N$. Calculated: equiv. weight 73.14.

Unsym-methylisopropylhydrazine. From 102 g (1 g-mole) of methylisopropylnitrosamine we obtained 500 ml of alkaline distillate, which was salted out with 280 g of sodium hydroxide.

The yield of the fraction corresponding to pure methylisopropylhydrazine was 35 g (39.8%):

B. p. 101.3-101.7° (769 mm), $d^{20}_4$ 0.8096, $n^{20}D$ 1.4234.

Found: equiv. weight 85.2, 86.5. $C_4H_{10}N_2H_2$. Calculated: equiv. weight 88.15.

Unsym-methylisopropylhydrazine is not described in the literature.

In addition, we obtained 13.1 g of a fraction with b. p. 93.8-101.3° ($d^{20}_4$ 0.8346, $n^{20}D$ 1.4254), which was wet methylisopropylhydrazine; analyzed as 96% pure hydrazine. Another 4.37 g of methylisopropylhydrazine was contained in the intermediate fraction with b. p. 52-93.8° (3 g, $n^{20}D$ 1.4069) and distillation residue.

We obtained 5.9 g of the 1st (amine) fraction: b. p. 50.2-52° (769 mm), $d^{20}_4$ 0.7042, $n^{20}D$ 1.3842, equiv. weight 73.8. The constants of this fraction are in complete agreement with those of methylisopropylamine.

Unsym.-methyl-n-butylhydrazine. For reaction we took 87 g (0.75 g-mole) of the nitrosamine. The distillate (250 ml) was salted out with 80 g of sodium hydroxide. On distillation we obtained 46.9 g (61.3%) of pure methyl-n-butylhydrazine:

B. p. 128-128.2° (736 mm), $d^{20}_4$ 0.8028, $n^{20}D$ 1.4267.

Found: equiv. weight 102.5, 103.0. $C_5H_{12}N_2H_2$. Calculated: equiv. weight 102.2.

Literature [10]: B. p. 50.5-51° (38 mm), $d^{21.3}_4$ 0.8040, $n^{21.3}D$ 1.42586.

The intermediate fraction with b. p. 93-128° (4.8 g, $n^{20}D$ 1.4176) and the residue contained another 5.9 g of methyl-n-butylhydrazine.

The first fractions with b. p. 80.93° (7.7 g) were wet methyl-n-butylamine and contained 7 g of the amine

Unsym.-methylisobutylhydrazine. For reduction we took 48.8 g (0.42 g-mole) of the nitrosamine. The alkaline distillate (140 ml) was salted out with 45 g of sodium hydroxide. Fractional distillation of the mixed bases gave 22.9 g (53.5%) of methylisobutylhydrazine:

B. p. 115.4-115.9° (758 mm), $d^{20}_4$ 0.7930, $n^{20}D$ 1.4207.

Found: equiv. weight 102.8, 102.4. $C_5H_{12}N_2H_2$. Calculated: equiv. weight 102.2.

Unsym.-methylisobutylhydrazine is not described in the literature.

1-Methyl-1-isobutylsemicarbazide: m. p. 110.5-111.4°.

Found %: N 28.79, 28.90. $C_6H_{15}ON_3$. Calculated %: N 28.93.

Literature [5]: m. p. 99°.

The intermediate fraction with b. p. 83-115.4° (7.4 g, $n^{20}D$ 1.4147) and the distillation residue (5 g) contained another 9.6 g methylisobutylhydrazine.

The 1st fraction with b. p. 75.5-83° (1.2 g, $d^{20}_4$ 0.7662, $n^{20}D$ 1.4008) was wet (89%) methylisobutylamine.

Dimethylhydrazine hydrochloride. Unsym.-dimethylhydrazine, despite its low boiling point, slowly distilled from the alkaline reaction mixture, probably due to formation of the hydrate. Salting out of the obtained dilute distillate with alkali (as in the above described syntheses) is not practical.

After the reduction of 74.1 g (1 g-mole) of dimethylnitrosamine the 600 ml of obtained distillate was neutralized (to methyl red) with 64.2 ml of concentrated hydrochloric acid. The solution was evaporated on the water bath, and the residue was dried in an oven for several hours at a temperature up to 120°. We obtained 74 g (77%) of the hydrochloride (see [4]).

The reduction of methylphenylnitrosamine was accompanied by a darkening of the reaction mixture and the formation of nitrogen oxides. The product was isolated in the usual manner and distilled completely at 90° (20 mm), did not reduce Fehling solution, and was pure methylaniline:

B. p. 195.3-196.1° (760 mm), $d^{20}_4$ 0.9863, $n^{20}D$ 1.5712. Literature data for N-methylaniline [11]: b. p. 196.2° (760 mm), $d^{20}_4$ 0.9862, $n^{20}D$ 1.5710.

From 102 g (0.75 g-mole) of methylphenylnitrosamine we obtained 57.3 g (71%) of methylaniline.

## SUMMARY

1. A simple method for the synthesis of dialkylhydrazines was proposed, based on the reduction of nitrosamines with zinc amalgam in hydrochloric acid medium.

2. The following homologs of unsym-dimethylhydrazine were synthesized and characterized by determining their physical constants: diethylhydrazine, di-n-propylhydrazine, di-n-butylhydrazine, methyl-n-butylhydrazine, methylisobutylhydrazine, methyl-n-propylhydrazine and methylisopropylhydrazine. The last three compounds are new.

3. It was shown that increasing the length of the alkyl radicals leads to some reduction in the yield of hydrazines and a simultaneous increase in the yield of secondary products — the secondary amines.

Methylphenylnitrosamine under the indicated reduction conditions is converted to methylaniline.

## LITERATURE CITED

[1] E. Fischer, Ber. 8, 1587, 1641 (1875).

[2] E. Fischer, Lieb. Ann. 199, 281 (1879).

[3] E. Fischer, Lieb. Ann. 190, 67 (1878); 236, 198 (1886).

[4] Organic Syntheses [Russian translation] Vol. 2, p. 199 (1949).

[5] R. Stoermer and V. Lepel, Ber. 29, 2110 (1896).

[6] A. I. Vogel and others, J. Chem. Soc. 514 (1952).

[7] H. Zimmer, L. F. Audrieth, M. Zimmer and R. A. Rowe, J. Am. Chem. Soc. 77, 790 (1955).

[8] J. Houben, Methods of Organic Chemistry [Russian translation] Vol. 4, Part 1, p. 144 (1949).

[9] Organic Syntheses [Russian translation] Vol. 2, p. 372 (1949).

[10] J. W. Brühl, Ber. 30, 158 (1897).

[11] B. V. Ioffe, Manual on Refractometry for Chemists [in Russian] (Izd. LGU, 1956).

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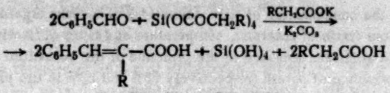
# TETRAACYLOXYSILANES IN ORGANIC SYNTHESES

## XIV.* SYNTHESIS OF HOMOLOGS OF CINNAMIC ACID (α-ALKYL-β-PHENYLACRYLIC ACIDS)

Iu. K. Iur'ev, G. B. Eliakov and A. N. Vysokosov

In a previous paper [1] we communicated that tetraacetoxysilane, the mixed anhydride of silicic and acetic acids, can successfully replace acetic anhydride in the synthesis of aromatic α,β-unsaturated acids by the Perkin reaction. Tetraacetoxysilane condenses with benzaldehyde in the presence of the conventionally used condensing agents – anhydrous potassium or sodium acetate, and also in the presence of potash, and here cinnamic acid is obtained in yields at least equal to those obtained with acetic anhydride.

In connection with this it seemed of great interest to investigate the possibility of utilizing the silicoanhydrides of other saturated monobasic organic acids to obtain homologs of cinnamic acid. In this paper we condensed the silicoanhydrides of propionic, butyric, valeric, isovaleric and caproic acids with benzaldehyde and obtained a number of α-alkyl-β-phenylacrylic acids in yields ranging from 29 to 69.5%.



$$2C_6H_5CHO + Si(OCOCH_2R)_4 \xrightarrow[K_2CO_3]{RCH_2COOK}$$

$$\longrightarrow 2C_6H_5CH{=}\underset{\displaystyle R}{\underset{|}{C}}{-}COOH + Si(OH)_4 + 2RCH_2COOH$$

(R = $CH_3$, $C_2H_5$, n-$C_3H_7$, n-$C_4H_9$).

When benzaldehyde was condensed with the silicoanhydrides of propionic, butyric and valeric acids under certain conditions we obtained only the corresponding α-alkylcinnamic acids, whereas in the case of using the silicoanhydride of isovaleric acid we obtained only the styrene homolog – 1-phenyl-3-methyl-1-butene in up to 70% yield. It should be mentioned that such a yield of 1-phenyl-3-methyl-1-butene is obtained only when the reaction is run under extremely drastic conditions (190-230°). However, it proves impossible to obtain α-isopropylcinnamic acid even under considerably milder conditions (100°, 20 hours of heating): a part of the benzaldehyde is recovered unchanged, and 1-phenyl-3-methyl-1-butene is the solitary reaction product, but its yield drops to 30%. From the literature it is known [2] that the main product in the condensation of benzaldehyde with the anhydride of isovaleric acid is also 1-phenyl-3-methyl-1-butene, together with the formation of only small amounts of α-isopropylcinnamic acid.

When the silicoanhydrides of butyric and caproic acids were condensed with benzaldehyde the corresponding styrene homologs – 1-phenyl-1-butene and 1-phenyl-1-hexene were formed as secondary reaction products (8.5-23%) in those cases where higher temperatures and a long heating time were employed.

The unsaturated hydrocarbon is formed together with the substituted cinnamic acid also when the anhydrides of the acids are used. Thus, 1-phenyl-2-methyl-1-propene [3] is formed when a mixture of isobutyric anhydride and benzaldehyde is heated in the presence of sodium isobutyrate at 150°. Its formation is explained as due to the decarboxylation of the intermediate addition product of the acid anhydride to benzaldehyde [4], since the α-isoalkylcinnamic acids as such are stable when heated above 100°.

α-Isobutylcinnamic acid was obtained by the condensation of benzaldehyde with either sodium or potassium isocaproate and acetic anhydride [5]. At the same time the reaction of isovaleric anhydride with benzaldehyde in the presence of sodium isovalerate gives α-isopropylcinnamic acid in very poor yield (7%) [2], since here carbon dioxide is evolved from the reaction mixture even at 70°, and 1-phenyl-3-methyl-1-butene is obtained as the main product.

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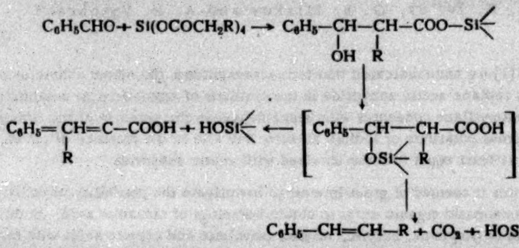
* For XI see J. Gen. Chem. 26, 926 (1956); for XII see Bull. Moscow State Univ., Phys. Chem. Series No. 1, 197 (1956).

The formation of 1-phenyl-3-methyl-1-butene in the condensation of the silicoanhydride of isovaleric acid with benzaldehyde must also be attributed to decarboxylation of the intermediate addition product of the silicoanhydride of the organic acid to benzaldehyde.

In this connection a more probable (than that given earlier [1]) scheme for the condensation of a tetraacyloxysilane with benzaldehyde should be regarded to be that scheme which includes the intermediate formation of their addition product, with its subsequent isomerization to the ester of orthosilicic acid and α-alkyl-β-phenyl-β-hydroxyhydracrylic acid, which cleaving only the silicic acid yields the α-alkyl-β-phenylacrylic acid, and the styrene homolog when both decarboxylation and cleavage of the silicic acid occur:



Consequently, also in the formation of secondary reaction products the silicoanhydrides of saturated monobasic organic acids behave in the Perkin reaction in exactly the same manner as do the corresponding anhydrides. As a result, each case involving the condensation of silicoanhydrides of various organic acids with benzaldehyde requires its own reaction conditions (ratio of reactants, temperature and time of heating), in which connection higher yields of α-alkylcinnamic acids are obtained in the presence of the potassium salt of the acid found in the silicoanhydride than in the presence of potash (respectively 68% and 53% in the preparation of α-ethylcinnamic acid, and 36% and 22% in the preparation of α-n-butylcinnamic acid).

## EXPERIMENTAL

To prepare the silicoanhydrides of the organic acids we charged 4 g-moles of the acid into a 500-ml round-bottomed flask fitted with reflux condenser and calcium chloride tube, then added 1.1-1.15 g-moles of silicon tetrachloride, mixed, and allowed to stand for 1-2 hours at 20°. Then the mixture was heated, at first on the water bath, and then with a low flame until the evolution of hydrogen chloride, which should proceed uniformly and not too vigorously, had ceased completely. Complete removal of the hydrogen chloride can be achieved by passing a stream of dry air through the hot silicoanhydride.

On cooling, the silicoanhydride was obtained at times as a solid mass (silicocaproic anhydride solidified even while hot), and at times as a gel, which was used as such to synthesize the α-alkylcinnamic acids [1].

Method of operation. In a 100-ml round-bottomed flask, fitted with reflux condenser and a stirrer descending through the condenser, was placed 0.1-0.2 g-mole of benzaldehyde and correspondingly 0.1-0.24 g-mole of the tetraacyloxysilane and 0.1-0.2 g-mole of either. anhydrous potash or anhydrous potassium salt of the acid found in the tetraacyloxysilane. The mixture was mixed thoroughly and heated in an oil bath with constant stirring. If the reaction mixture solidified at the start, then the temperature was raised in several minutes to 20-30° above that chosen.

On conclusion of reaction the mass was cooled, treated with warm 2N sodium hydroxide solution until weakly alkaline (to litmus),* and the unchanged benzaldehyde steam-distilled. The residue in the flask was treated with activated carbon, boiled, steam passed through for 5 minutes, and then suction-filtered hot. The precipitate on the filter was washed twice with small portions of 2N sodium hydroxide solution, then with warm water, and the acid was isolated from the combined filtrates by acidification with concentrated hydrochloric acid. The α-alkylcinnamic acids were usually obtained quite pure; they were recrystallized from anhydrous alcohol.

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* An excess of caustic should be avoided to prevent contamination of the reaction product with silicic acid.

To isolate the styrene homolog, the distillate from the steam-distillation was saturated with common salt and then extracted with ether. The ether extract was washed with sodium bisulfite, then with alkali, and dried over calcium chloride. After removal of the ether by distillation the hydrocarbon was vacuum-distilled.

α-Methylcinnamic acid. A mixture of 10.6 g of benzaldehyde, 44 g of silicopropionic anhydride and 13.8 g of potash was heated for 12 hours at 190-195°. We obtained 11.2 g (69.5%) of α-methylcinnamic acid with m. p. 81-81.2°.

Found %: C 74.14, 74.20; H 6.25, 6.28. $C_{10}H_{10}O_2$. Calculated %: C 74.05; H 6.21.

Literature: m. p. 81° or 74° (due to the existence of two crystalline modifications) [6].

α-Ethylcinnamic acid. a) A mixture of 10.6 g of benzaldehyde, 37.6 g of silicobutyric anhydride and 13.8 g of potash was heated for 14 hours at 160-170°. We obtained 9.3 g (53%) of α-ethylcinnamic acid with m. p. 106°.

Found %: C 75.30, 75.32; H 7.08; 7.05. $C_{11}H_{12}O_2$. Calculated %: C 74.97; H 6.86.

Literature: m. p. 104° [6], 104-105° [7].

We also isolated 1.9 g (14.5%) of 1-phenyl-1-butene: b. p. 84-85° (20 mm), $n^{20}D$ 1.5384, $d^{20}_4$ 0.9099, $MR_D$ 45.46. $C_{10}H_{12}F_4$. Calculated 44.31.

Literature: b. p. 77° (10 mm), $n^{20}D$ 1.5387, $d^{20}_4$ 0.9106 [8]; b. p. 89-90° (15 mm), $n^{16}D$ 1.5414, $d^{16}_4$ 0.9124 [9]. 1-Phenyl-1,2-dibromobutane, obtained by reaction with bromine in chloroform, melted at 70°.

Found %: Br 54.64, 54.55. $C_{10}H_{12}Br_2$. Calculated %: Br 54.73.

Literature: m. p. 70° [10]; 71° [11].

b) The heating of a mixture of 36.8 g of silicobutyric anhydride, 10.6 g of benzaldehyde and 13.8 g of potash for 5 hours at 185-190° gave 8.4 g (48%) of α-ethylcinnamic acid with m. p. 106°, and 2.7 g (20%) of 1-phenyl-1-butene with b. p. 65-67° (7 mm) and $n^{20}D$ 1.5386.

c) The heating of a mixture of 10.6 g of benzaldehyde, 37.6 g of silicobutyric anhydride and 12.6 g of potassium butyrate gave 11.9 g (68%) of α-ethylcinnamic acid; m. p. 106°. The mixed melting point with the acid obtained from the preceding experiments was not depressed.

α-Propylcinnamic acid. A mixture of 10.6 g of benzaldehyde, 34.5 g of silicovaleric anhydride and 13.8 g of potash was heated for 5.5 hours at 185-190°. We obtained 5.5 g (29%) of α-propylcinnamic acid with m. p. 92.8-93°.

Found %: C 76.04, 76.02; H 7.52, 7.64. $C_{12}H_{14}O_2$. Calculated %: C 75.76; H 7.41.

Literature: m. p. 93° [12].

As shown in the preceding series of experiments, there is no doubt but that both a reduction in the temperature and an increase in the time of heating should favor an increase in the yield of acid.

1-Phenyl-3-methyl-1-butene. A mixture of 10.6 g of benzaldehyde, 64 g of silicovaleric anhydride and 13.8 g of potash was heated for 14 hours (9 hours at 190° and 5 hours at 230°). We obtained 10.42 g (70%) of 1-phenyl-3-methyl-1-butene.

B. p. 91-92.5° (17 mm), $n^{20}D$ 1.5228, $d^{20}_4$ 0.8901, $MR_D$ 50.17. $C_{11}H_{14}F_4$. Calculated 48.93.

Found %: C 90.21, 90.33; H 9.71, 9.69. $C_{11}H_{14}$. Calculated %: C 90.27; H 9.63.

Dibromide: m. p. 129-129.2°.

Found %: C 43.23, 43.35; H 4.69, 4.79; Br 51.99, 52.15. $C_{11}H_{14}Br_2$. Calculated %: C 43.17; H 4.61; Br 52.21.

Literature: b. p. 207° (757 mm); 102-103° (26 mm), $n^{14.6}D$ 1.5248, $d^{14.6}_4$ 0.8903 [9]; b. p. 94-105° (11 mm), $n^{20}D$ 1.5251, $d^{20}_4$ 0.887 [13]; dibromide: m. p. 125° [10].

α-Butylcinnamic acid. a) A mixture of 10.6 g of benzaldehyde, 37.5 g of silicocaproic anhydride and 13.8 g of potash was heated for 10 hours at 160-165°. We obtained 4.5 g (22%) of α-butylcinnamic acid with m. p. 83.7°.

Found %: C 76.64, 76.61; H 8.07, 8.20. $C_{13}H_{16}O_2$. Calculated %: C 76.48; H 7.90.

Literature: m. p. 83-84° [4], m. p. 80° [12].

b) A mixture of 10.6 g of benzaldehyde, 48.9 g of silicocaproic anhydride and 19 g of potassium n-caproate was heated for 15 hours at 175-180°. We obtained 7.4 g (36%) of α-butylcinnamic acid; m. p. 83.5°.

The mixed melting point with the acid obtained from the preceding experiment was not depressed.

The secondary reaction product obtained here in 23% yield was a hydrocarbon fraction, which from its boiling point corresponded to 1-phenyl-1-pentene.

B. p. 116-121° (22 mm), $n^{20}D$ 1.5182, $d^{20}_4$ 0.9028.

Literature: b. p. 82° (9 mm), $d^{20}_4$ 0.892, $n^{15}D$ 1.5139 [14].

## SUMMARY

1. It is possible to use the silicoanhydrides of aliphatic acids in place of the anhydrides of the corresponding acids in the condensation with benzaldehyde, leading to the formation of α-alkylcinnamic acids.

2. Only the corresponding cinnamic acids are obtained when the silicoanhydrides of propionic and valeric acids are employed; β-isopropylstyrene is the main reaction product when the silicoanhydride of isovaleric acid is utilized; together with α-alkylcinnamic acids, the corresponding styrenes are obtained as secondary reaction products when the silicoanhydrides of butyric and caproic acids are employed.

3. Higher yields of α-alkylcinnamic acids are obtained in the presence of the anhydrous potassium salt of the acid found in the silicoanhydride than in the presence of potash.

## LITERATURE CITED

[1] Iu. K. Iur'ev, G. B. Eliakov and A. N. Vysokosov, J. Gen. Chem. 26, 926 (1956).*

[2] A. Schaarschmidt, E. Georgeacopol and J. Herzenberg, Ber. 51, 1059 (1918).

[3] W. Perkin, J. Chem. Soc. 35, 138 (1879).

[4] D. Breslow and C. Hauser, J. Am. Chem. Soc. 61, 786, 793 (1939).

[5] A. Michael, Ber. 34, 918 (1901).

[6] W. Perkin, J. Chem. Soc. 31, 393 (1877).

[7] F. Fichter and E. Alber, J. pr. Ch. [2] 74, 337 (1906).

[8] C. Riiber, Ber. 44, 2393 (1911).

[9] A. Klages, Ber. 37, 2316 (1904).

[10] J. Levy and F. Dvoleitzka-Gombinska, Bull. Soc. Chim. 49, 1765 (1931).

[11] R. Ia. Levina and N. A. Shcheglova, J. Gen. Chem. 11, 527 (1941).

[12] M. Bogert and D. Davidson, J. Am. Chem. Soc. 54, 334 (1932).

[13] F. Kunckell and K. Stahel, Ber. 37, 1088 (1904).

[14] A. Klages, Ber. 39, 2592 (1906).

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# TRANSAMINATION REACTIONS OF CARBOXYLIC ACID AMIDES

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An investigation of the reversible transamination of carboxylic acid amides, proceeding by the equation

$$RCONHR' + R''NH_2 \rightleftharpoons RCONHR'' + R'NH_2,$$

originated from the paper [1], where it was shown that transamination occurs when substituted ureas are reacted with primary amines, leading to the formation of a new substituted urea and a new amine

$$2NH_2R' + R''HNCONHR'' \rightleftharpoons 2NH_2R'' + R'HNCONHR'$$

Thus, for example, the reaction of N,N'-dipyridylurea with aniline gave N,N'-diphenylurea and aminopyridine. The indicated authors studied 7 pairs of a similar type of reversible reactions. To expand on this study we thought it would be interesting to investigate the transamination of carboxylic acid amides. First we studied the reaction of acetamide with aromatic amines and established that hydrogen chloride facilitates a shift in the equilibrium of this reversible reaction. For example, the heating of acetamide with aniline for 8 hours at 180-230° under the conditions described by Kelbe [2] yields a small amount of acetanilide, while in the presence of hydrogen chloride the same reaction leads to the quantitative formation of acetanilide in 45 minutes. When acetamide was reacted (in the presence of hydrogen chloride) with o-toluidine, and also with p-aminodimethylaniline, we obtained the corresponding acetyl derivatives in good yield, which makes the reaction of acetamide with aromatic amines a potentially useful method of acylation in certain cases.

A number of authors have attempted to react substituted amides with aromatic amines, but they were able to effect a shift of the equilibria of these reactions only under extremely drastic conditions. Thus, for example, a shift of the equilibrium of the reaction

$$CH_3CONHC_6H_{11} + RNH_2 \rightleftharpoons CH_3CONHR + C_6H_{11}NH_2$$

was achieved only by heating the reaction mixture for 2-5 days at 260° in dodecylpiperidine solution at a pressure of 100 atm [3].

The heating of acetanilide and p-anisidine for 13 hours gave aniline and p-acetanisidide, in which connection the presence of the p-acetanisidide was established spectrophotometrically [4].

We found that in the presence of hydrogen chloride the equilibrium of the reversible reaction

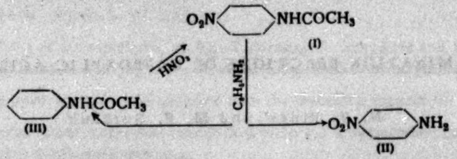
$$CH_3CONHR + R'NH_2 \rightleftharpoons CH_3CONHR' + RNH_2$$

is shifted in 45 minutes at 180-190° almost completely from left to right. We ran a number of transamination reactions, proceeding by the scheme

$$RNHCOCH_3 + R'NH_2 \rightleftharpoons R'NHCOCH_3 + RNH_2$$

In five of the reactions R' = $C_6H_5$, and R = o-$CH_3C_6H_4$, p-$(CH_3)_2NC_6H_4$, p-$CH_3OC_6H_4$, p-$CH_3C_6H_4$, p-$O_2NC_6H_4$; in one reaction R' = o-$CH_3C_6H_4$ and R = $C_6H_5$.

In all of these reactions we obtained the newly formed substituted amide and primary amine in nearly quantitative yield, which could be easily separated due to their different solubility in water. The reactions of aromatic amines with carboxylic acid amides can be used as a method for the simultaneous preparation of substituted amides and primary aromatic amines. Some of these reactions can be utilized in industry. For example, the reaction of p-nitroacetanilide with aniline can serve as a base for the commercial preparation of p-nitroaniline, operated as a cyclic process by the scheme



This process is economical for the reason that both the final reaction product, p-nitroaniline (II), and the starting product, acetanilide (III), which is used in the same cyclic process to obtain p-nitroaniline, are formed simultaneously at the stage of heating p-nitroacetanilide (I) with aniline. The advantage of the proposed method for obtaining p-nitroaniline over the present method of manufacture, proceeding in 3 stages by the scheme

$$C_6H_5NH_2 \xrightarrow{(CH_3CO)_2O} C_6H_5NHCOCH_3 \xrightarrow{HNO_3} p\text{-}O_2NC_6H_4NHCOCH_3 \xrightarrow{H_2SO_4} p\text{-}O_2NC_6H_4NH_2$$

consists in a reduction of the number of steps to two and a corresponding decrease in the consumption of aniline, acetic anhydride sulfuric acid and other raw materials. It is possible to obtain sulfanilamide (white streptocide) on a commercial scale by a similar scheme. The method used in the pharmaceutical industry at the present time to obtain sulfanilamide, proceeding in 4 stages by the scheme

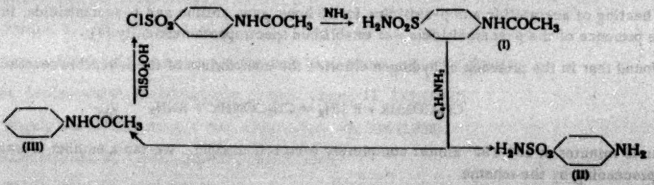
$$C_6H_5NH_2 \xrightarrow{(CH_3CO)_2O} C_6H_5NHCOCH_3 \xrightarrow{HOSO_2Cl} p\text{-}ClO_2SC_6H_4NHCOCH_3 \xrightarrow{NH_3}$$
$$\rightarrow p\text{-}H_2NO_2SC_6H_4NHCOCH_3 \xrightarrow{H_2SO_4} p\text{-}H_2NO_2SC_6H_4NH_2$$

is complicated and requires the consumption of a large number of starting products.

We developed a new method for the preparation of sulfanilamide, also based on the transamination reaction discovered by us

$$\underset{(I)}{p\text{-}H_2NO_2SC_6H_4NHCOCH_3} + C_6H_5NH_2 \rightleftharpoons \underset{(II)}{p\text{-}H_2NO_2SC_6H_4NH_2} + \underset{(III)}{C_6H_5NHCOCH_3}$$

The method proposed by us for the preparation of sulfanilamide, proceeding in three stages as a cyclic process by the scheme



is economical in that both the final product, sulfanilamide (II), and the starting product, acetanilide (III), are formed simultaneously at the stage of heating p-acetamidobenzenesulfonamide (I) with aniline, which leads to a reduction in the number of steps from 4 to 3 and a corresponding decrease in the consumption of aniline, acetic anhydride, sulfuric acid and other raw materials.

## EXPERIMENTAL

Reaction of acetamide with the hydrochlorides of primary aromatic amines. Dry hydrogen chloride was passed into a solution of 1.5 g of acetamide in 20 ml of aniline for 15-20 minutes, and then the reaction mixture was heated in an oil bath at 180-190° for 45 minutes. The mixture after cooling was treated with 20 ml of 25% aqueous ammonia solution and then steam was passed into it. The solution after removal of the aniline by steam-distillation was cooled to give crystals with m. p. 114°. The mixed melting point with authentic acetanilide was not depressed. Yield 82%. In a similar manner the reaction of acetamide (1.5 g) with o-toluidine (30 ml) under the same conditions gave o-acetotoluidide; yield 46%. p-Acetamidodimethylaniline was obtained in 78% yield when 1.5 g of acetamide was heated with 4.37 g of p-aminodimethylaniline hydrochloride (180-190°, 45 minutes).

Reaction of acylarylamides with hydrochlorides of primary aromatic amines. A stream of dry hydrogen chloride was passed into a solution of 2 g of p-nitroacetanilide in 30 ml of aniline for 15-20 minutes, and then the reaction mixture was heated for 45 minutes in an oil bath at 180-190°. The mixture after cooling was treated with 20 ml of 25% aqueous ammonia solution and then steam-distilled. After removal of the aniline by steam-distillation the aqueous solution was cooled to give a crystalline substance with m. p. 147°, which did not depress the melting point when mixed with authentic p-nitroaniline. Evaporation of the mother liquor gave a crystalline substance, which did not depress the melting point when mixed with authentic acetanilide. The yield was nearly quantitative.

Under the same conditions the reaction of aniline (20 ml) with o-acetotoluidide (2 g) gave acetanilide and o-toluidine in quantitative yield. The reaction of aniline (25 ml) with 2.5 g of p-acetanisidide led to the formation of acetanilide and p-anisidine. In a similar manner, the reaction of aniline (25 ml) with p-acetamidobenzenesulfonamide (3 g), with p-acetamidodimethylaniline (2 g), and with p-acetotoluidide (3 g), gave in all cases acetanilide and respectively p-aminobenzenesulfonamide, p-aminodimethylaniline (80% yield) and p-toluidine. The reaction under the same conditions of o-toluidine (30 ml) with p-nitroacetanilide (2 g), and also with acetanilide (3 g), led in both cases to the formation of o-acetotoluidide and respectively p-nitroaniline (quantitative yield) and aniline (75% yield).

## SUMMARY

The following was established when the transamination of carboxylic acid amides was studied on a number of examples.

1. The reaction of acetamide with the hydrochlorides of aromatic amines yields the corresponding acylamide and ammonia.

2. The heating of the hydrochlorides of primary aromatic amines with acylarylamides yields a new acylarylamide and a new aromatic amine.

3. It is possible to utilize individual transamination reactions in the commercial production of certain amines. In the production of p-nitroaniline the authors recommend saponifying p-nitroacetanilide not with sulfuric acid, as is the practice at the present time, but instead with aniline, which leads to the simultaneous formation of both the final product p-nitroaniline and the starting product acetanilide, the latter being used in the same cyclic process to obtain p-nitroaniline. Similarly in the production of sulfanilamide the authors recommend saponifying the p-acetamidobenzenesulfonamide with aniline, which leads to the simultaneous formation of both sulfanilamide and starting acetanilide.

## LITERATURE CITED

[1] M. P. Gerchuk, D. A. Lifshits and S. Z. Taits, J. Gen. Chem. 20, 924 (1950).*

[2] W. Kelbe, Ber. 16, 1199 (1883).

[3] M. E. Smith and H. Adkins, J. Am. Chem. Soc. 60, 657 (1938).

[4] R. Jaunin, Helv. Chim. Acta 35, 1414 (1952).

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# MECHANISM OF THE REDUCTION OF $\gamma$-ACETOBUTYRONITRILE

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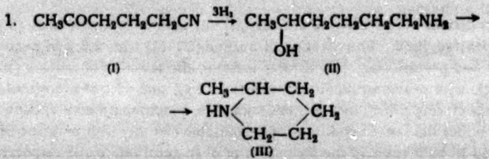
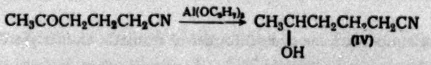
The reduction of $\gamma$-acetobutyronitrile (I) with sodium in butyl alcohol [1] yields two reaction products – 6-amino-2-hexanol (II, 17%) and 2-methylpiperidine (III, 15%).

S. M. Gurvich [2] postulated that the reduction proceeds according to scheme 1.


1. CH₃COCH₂CH₂CH₂CN
3H₂
CH₃CHCH₂CH₂CH₂CH₂NH₂
OH
(I)
(II)
CH₃–CH–CH₂
HN
CH₂
CH₂–CH₂
(III)

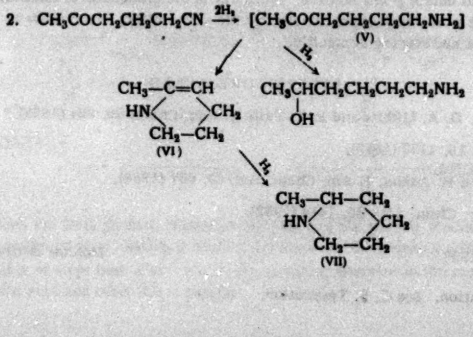
In order to increase the yield of needed 6-amino-2-hexanol we subjected $\gamma$-acetobutyronitrile to stepwise hydrogenation. The carbonyl group was reduced first, using the Meerwein-Pondorf method [3], and this gave $\delta$-hydroxycapronitrile (IV, 84%).



$$CH_3COCH_2CH_2CH_2CN \xrightarrow{Al(OC_3H_7)_3} CH_3\underset{OH}{CH}CH_2CH_2CH_2CN \quad (IV)$$

The latter was then reduced with sodium in isoamyl alcohol to 6-amino-2-hexanol (47.7%). It should be mentioned that the formation of 2-methylpiperidine was not observed here.

Our data do not agree with the above reaction scheme proposed by Gurvich and we postulate that the intermediate product in the reduction of $\gamma$-acetobutyronitrile with sodium in alcohol is 6-amino-2-hexanone (V), i.e., the process goes according to scheme 2.


2. CH₃COCH₂CH₂CH₂CN
2H₂
[CH₃COCH₂CH₂CH₂CH₂NH₂]
(V)
H₂
CH₃–C=CH
HN
CH₂
CH₂–CH₂
(VI)
CH₃CHCH₂CH₂CH₂CH₂NH₂
OH
H₂
CH₃–CH–CH₂
HN
CH₂
CH₂–CH₂
(VII)

To support our viewpoint we selectively reduced the CN group of γ-acetobutyronitrile in acetic anhydride using skeletal nickel catalyst. The 6-methyl-1,2,3,4-tetrahydropyridine (VI, 32% yield) obtained here was then reduced further with sodium in isoamyl alcohol to 2-methylpiperidine (VII, 74.5% yield). For identification purposes we prepared 6-methyl-1,2,3,4-tetrahydropyridine by the Gabriel method [4], which when reduced under similar conditions also gave 2-methylpiperidine. Gurvich considers the indicated reaction mechanism (scheme 2) to be impossible, citing the fact that tetrahydropyridines are not reduced by sodium in alcohol [2]. However, such applies only to the $\Delta^3$-tetrahydropyridines [5], whereas the $\Delta^2$-tetrahydropyridines are easily reduced to the corresponding piperidines [6].

Proceeding from the above, we believe that the reduction of γ-acetobutyronitrile proceeds through the intermediate stage of forming 6-amino-2-hexanone, which together with cyclization to 6-methyl-1,2,3,4-tetrahydropyridine, is simultaneously reduced to 6-amino-2-hexanol, i.e., the reaction goes according to the second scheme.

## EXPERIMENTAL

γ-Acetobutyronitrile was obtained by the cyanoethylation of either acetone [1] or acetoacetic ester [7], and had the following constants:

B. p. 93-96° at 6 mm, 236-238° at 744 mm; $n^{20}D$ 1.4325, $d^{20}_4$ 0.968, $MR_D$ 29.68.

δ-Hydroxycapronitrile. To a boiling solution of 67 g of aluminum isopropylate in 150 ml of anhydrous isopropyl alcohol was added 17.5 g of γ-acetobutyronitrile. The reduction was run for 1 hour and 40 minutes. Then the reaction mass was worked up in the usual manner [3]. The obtained cyanohydrin was repeatedly extracted with ether, and the ether solution was washed with saturated magnesium sulfate solution and then dried. After removal of the ether by distillation the residue was vacuum-distilled. B. p. 106-108° at 4 mm, yield 15 g (84.2%). Light-yellow mobile liquid, readily soluble in water, and giving a negative test for the keto group.

$n^{20}D$ 1.4420, $d^{20}_4$ 0.9641, $MR_D$ 31.0; calculated 31.25.

Found %: N 12.37, 12.17. $C_6H_{11}ON$. Calculated %: N 12.39.

6-Amino-2-hexanol. Twenty-three grams of sodium metal was added in 40 minutes to a boiling solution of 17 g of δ-hydroxycapronitrile in 450 ml of isoamyl alcohol. The mixture was heated until all of the sodium had dissolved. After cooling, the mixture was treated with water and then with concentrated hydrochloric acid until acid to Congo. The isoamyl alcohol and water were removed in vacuo, and the residue, a thick slurry, was heated with alcohol. The alcohol solution was filtered from insoluble salts, and then evaporated in vacuo to dryness. The residue was treated with 40% sodium hydroxide, and the separated base was extracted with chloroform. The chloroform solution was dried over potash. After removal of the chloroform by distillation we obtained 8.5 g (47.7%) of 6-amino-2-hexanol with b. p. 96-97° at 5 mm. The substance is a strongly alkaline colorless liquid, readily soluble in water, alcohol and chloroform, and difficultly soluble in ether.

$n^{20}D$ 1.4605, $d^{20}_4$ 0.9210, $MR_D$ 34.76; calculated 34.98.

Found %: N 12.13, 12.20. $C_6H_{15}ON$. Calculated %: N 11.96.

Reaction of 6-amino-2-hexanol with thionyl bromide at 4-8° gave 2-bromo-6-aminohexane hydrobromide. The latter had m. p. 95-102° (in a sealed capillary), is readily soluble in water, alcohol and acetone, and is insoluble in ether and benzene.

Found %: N 5.18; 5.26. $C_6H_{15}NBr_2$. Calculated %: N 5.36.

6-Methyl-1,2,3,4-tetrahydropyridine. A solution of 5 g of γ-acetobutyronitrile in 20 ml of acetic anhydride was hydrogenated for 4 hours in the presence of skeletal nickel catalyst (3.5 g) at room temperature and a pressure of 1.5 atm. After removal of the catalyst the excess acetic anhydride was vacuum-distilled. The residue was boiled with 20% hydrochloric acid for 4 hours, after which the solution was evaporated to dryness. The obtained crystalline precipitate was treated with boiling anhydrous alcohol, the alcohol solution was concentrated, the residue was treated with 40% sodium hydroxide solution, and the separated base was extracted with ether. After removal of the ether by distillation we collected the fraction with b. p. 130-132° at 747 mm, $n^{20}D$ 1.4560. Yield 1.4 g (32.1%).

The colorless liquid is soluble in water, alcohol and ether. It darkens on standing. Picrate (from alcohol), m. p. 120.5-121°. The mixed melting point with the picrate of the 6-methyl-1,2,3,4-tetrahydropyridine obtained by the Gabriel method [4] was not depressed. The mixed melting point with the picrate of 2-methylpiperidine was depressed.

2-Methylpiperidine. Sodium metal (7 g) was added to a boiling solution of 2.9 g of 6-methyl-1,2,3,4-tetrahydropyridine in 100 ml of isoamyl alcohol. As a reaction result we obtained 2.2 g (74.5%) of 2-methylpiperidine with b. p. 115-117° and $n^{20}D$ 1.4475. The picrate after recrystallization from water had m. p. 132-132.5°, and the hydrochloride had m. p. 209.5-210.5°. The mixed melting point with authentic 2-methylpiperidine hydrochloride was not depressed.

## SUMMARY

1. It was found that the stepwise reduction of γ-acetobutyronitrile increases the yield of 6-amino-2-hexanol from 17 to 40%.

2. It was shown that the reduction of γ-acetobutyronitrile with sodium in alcohol proceeds through the intermediate stage of forming 6-amino-2-hexanone, which together with cyclization to 6-methyl-1,2,3,4-tetrahydropyridine, with subsequent reduction to 2-methylpiperidine, is simultaneously reduced to 6-amino-2-hexanol.

## LITERATURE CITED

[1] A. P. Terent'ev and S. M. Gurvich, J. Gen. Chem. 21, 1632 (1951).*

[2] S. M. Gurvich, Dissertation "Use of Acrylonitrile in the Synthesis of Nitrogen-Containing Heterocyclic Compounds" (Moscow State University 1951).**

[3] Organic Reactions [Russian translation] Vol. 2, p. 197 (1950).

[4] S. Gabriel, Ber. 42, 1242 (1909).

[5] W. Koenigs, Ber. 40, 3202 (1907).

[6] A. Lipp, Ber. 25, 2190 (1892)

[7] N. F. Alberston, J. Am. Chem. Soc. 72, 2594 (1950).

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Parasitology and Helminthology

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** In Russian.

# RESEARCH IN THE FIELD OF SYNTHETIC DYESTUFFS

## IX. SYNTHESIS OF BISAZO DYES BY THE CONDENSATION OF DIAZO COMPOUNDS WITH SALTS OF N-ARYL QUINALDINES

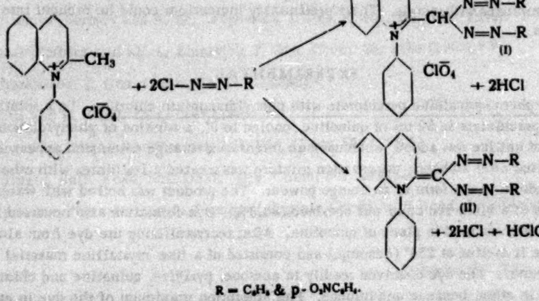
G. T. Piliugin and S. V. Shinkorenko

Among the numerous reactions of diazonium salts there are only a few investigations connected with the coupling of diazo compounds with heterocyclic methylene bases and with quaternary salts of heterocylic compounds. Coupling has been observed at an active methyl group with onium compounds of quinaldine and lepidine [1-4], with various heterocyclic bases and their salts [5, 6] and with monohydroxydihydropyrimidines [7]. The reactions have been investigated of diazonium salts with methylbenzimidole [8], with active methyl groups on heterocyclic compounds [9], with methylbenzthiazole [10] and with quaternary salts of heterocyclic nitrogen compounds containing active methyl groups in the $\alpha$- and $\gamma$- positions relative to the nitrogen [11].

While studying the chemical transformations of quaternary salts of derivatives of quinoline containing aromatic radicals on the hetero nitrogen atom, which we had prepared [12], interest arose in the coupling of these salts with diazonium compounds. Investigations of this type are not found in the literature. These salts, containing as they do electrophilic radicals, should couple relatively easily with diazohydrates, diazotates and diazonium salts with the formation of ionic dyes.

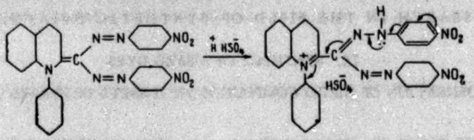
This communication is concerned with the coupling of N-phenylquinaldine perchlorate with phenyldiazonium chloride and with p-nitrophenyldiazonium chloride.

The azo coupling reaction could proceed according to the following schemes:

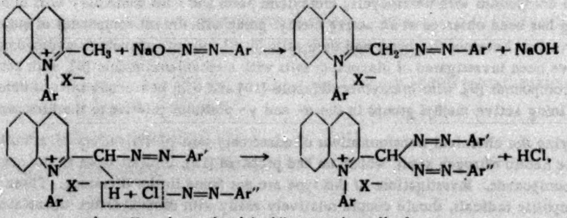


R = $C_6H_5$ & p-$O_2NC_6H_4$.

Investigation of the dyestuffs isolated showed that under our reaction conditions bis-(phenylazo)-N-phenyl-2-quinolinemethane perchlorate (I) with an absorption maximum at 458 mμ and bis-(p-nitrophenylazo)-N-phenyl-2-quinolinemethane (II) with an absorption maximum at 588 mμ, were formed. It is very strange that on coupling with the p-nitrophenyldiazonium salt a dye that does not contain an anion was formed whereas on coupling with the phenyldiazonium salt a salt-type dye was isolated. It must be assumed that the effect of the nitro group in the diazonium salt markedly weakens the basic character of the hetero nitrogen atom such that it is unable to form salts. It was noted that on addition of concentrated sulfuric acid to crystals of the dye a beautiful, intense blue coloration was formed. This phenomenon is connected with salt formation by an increase in the electrophilic character of the hetero nitrogen atom and by the redistribution of the electron density of the molecule as a whole, which is also the cause of the deepening in color.



It is interesting to note that similar bisazo dyes can be synthesized also by a stepwise method in two stages, which is of considerable value for the synthesis of bisazo dyes of an unsymmetrical structure.



where X-anion; Ar, Ar′, A″-aromatic radical

The preparation of bisazo dyes is also not devoid of practical interest. Thus on coupling (depending on the conditions) the dye remains in a soluble form and only on neutralizing with ammonia or sodium carbonate does it manifest itself in coming down as a precipitate. Experiments have shown that on impregnation of cotton or fabrics with the soluble components and subsequently treating with ammonia vapor or sodium carbonate solution the dye becomes fixed on the cotton. Moreover the separated dyes possess indicator properties, particularly those containing nitro groups in the molecule. There might also be some interest in the fact that these coloring materials form colored complexes with metals. These preliminary indications could be brought into practical use by suitable investigation.

## EXPERIMENTAL

Coupling of N-phenylquinaldine perchlorate with phenyldiazonium chloride. To a solution of 5.0 g of N-phenylquinaldine perchlorate in 50 ml of quinoline, cooled to 0°, a solution of phenyldiazonium chloride prepared from 3 ml of aniline was added, whereupon an intense red-orange coloration appeared immediately. No dye had precipitated after 10 hours; the reaction mixture was treated a few times with ether, as a result of which the dye came down in the form of an orange powder. The product was boiled with water for the removal of salts. 7.0 g of dye of a brick-red color was obtained (84.3%). Dye formation also occurred if glacial acetic acid or aqueous pyridine was used in place of quinoline. After recrystallizing the dye from alcohol and then from aqueous acetone it melted at 234° (decomp.) and consisted of a fine crystalline material of a brick-red color with a yellow luster. The dye dissolved readily in acetone, pyridine, quinoline and chloroform, and was practically insoluble in ether, benzene and toluene. The absorption maximum of the dye in ethanol was at 458 mμ. The absorption curve was plotted by a recording spectrophotometer SF-2M.

Found %: Cl 6.45, 6.37; N 13.40. $C_{28}H_{22}O_4N_5Cl$. Calculated %: Cl 6.71; N 13.26.

Coupling of N-phenylquinaldine perchlorate with p-nitrophenyl-diazonium chloride. To a solution of 5.0 g of phenylquinaldine perchlorate in 70 ml of glacial acetic acid a solution of p-nitrophenyldiazonium chloride, prepared from 4.3 g of p-nitroaniline, was added with cooling. After mixing the solutions no color change was observed even after some hours. On neutralizing with sodium carbonate a dye began to separate immediately in the form of a dark blue powder. The yield of crude product was 8.0 g (92.6%). For purification the substance was boiled with water a few times, reprecipitated from pyridine and recrystallized from alcohol-water. The dye, consisting of fine crystals of a dark blue color, with m. p. 209-210°, dissolved readily in pyridine, chloroform, acetone, acetic acid and dioxan; it was practically insoluble in ether, benzene and toluene. In concentrated sulfuric acid the dye dissolved with a pure blue color. The acetic acid solution was a red-orange color becoming blue with alkalis. It should be noted that this dye changes color depending on the solvent. Thus in pyridine, dioxan and chloroform it acquires a blue color, in alcohol and acetone – a violet, and in acetic acid and ethyl acetate a red-orange color. A similar phenomenon, called solvatochromism, is met with in many internally ionized coloring materials, the depth of color is connected with the nature of the dye and with the degree of polarization [13]. The absorption maximum of the dye in ethanol is at 588 mμ.

Found %: N 18.62, 18.63. $C_{28}H_{19}O_4N_7$. Calculated %: N 18.94.

## SUMMARY

1. The possibility has been shown of the interaction of salts of N-arylquinaldines at the α-methyl group with diazonium salts, with the formation of a new type of bisazo dye (two azo groups on one carbon atom).

2. The interaction of N-phenylquinaldine perchlorate with phenyldiazonium chloride and with p-nitrophenyldiazonium chloride has been studied. As a result two azo dyes have been isolated and characterized – bis(phenylazo)-N-phenyl-2-quinolinemethane perchlorate, with an absorption maximum at 458 mμ, and bis-(p-nitrophenyl-azo)-N-phenyl-2-quinolinemethane, with an absorption maximum at 588 mμ.

## LITERATURE CITED

[1] W. König, Ber. 56, 1543 (1923).

[2] W. König, Ber. 57, 891 (1924).

[3] Rasenhauer, Ber. 57, 1292 (1924).

[4] E. Königs and H. Bueren, J. pr. Ch. 146, 119 (1936).

[5] A. E. Porai-Koshitz, Iu. I. Aushkap and N. K. Amsler, SPb. Technol. Inst. 27, 109; J. Russ. Chem. Soc. 42, 518 (1936).

[6] A. E. Porai-Koshitz, Selected Works, Acad. Sci. USSR Press 229 (1949).*

[7] N. V. Khromov-Borisov and A. M. Savchenko, J. Gen. Chem. 22, 1680 (1952).**

[8] B. A. Porai-Koshitz and Kh. L. Muravich, J. Gen. Chem. 23, 1583 (1953).**

[9] A. A. Kharkharov, J. Gen. Chem. 23, 1175 (1953).**

[10] P. Francois and H. Whal, C. r. 1049 (1954).

[11] H. Whal and Le Bris, Marie-Therese, Bull, Soc. Chim. 587 (1954).

[12] G. T. Piliugin, Bull. Acad. Sci. USSR, Div. Chem. Sci. 253 (1952).**

[13] A. I. Kiprianov, "The Electronic Theory of Organic Chemistry," Acad. Sci. Ukrainian SSR Press, 163 (1949).*

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# RESEARCH IN THE FIELD OF SYNTHETIC DYESTUFFS

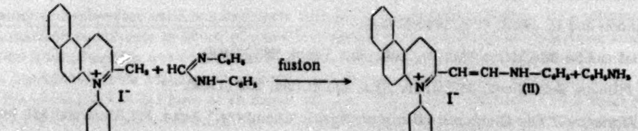
## X. SYNTHESIS OF N-ARYL-2-β-ANILINOVINYLQUINOLINE DERIVATIVES AND THEIR TRANSFORMATIONS

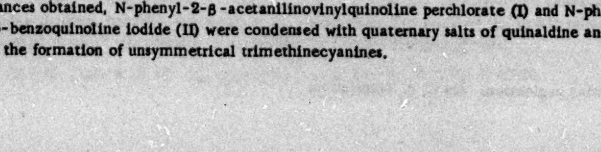
G. T. Piliugin, E. P. Opanasenko and S. V. Shinkorenko

For the synthesis of trimethinecyanine dyes of unsymmetrical structure substances prepared from diphenylformamidine and quaternary salts of heterocyclic bases are most often used [1, 2]. These intermediate products are prepared mainly from haloalkylates of methylbenzthiazole and trimethylindolenine, and much more rarely from other heterocyclic compounds. On condensing the above-mentioned substances with other quaternary salts unsymmetrical trimethinecyanines are obtained [3-7].

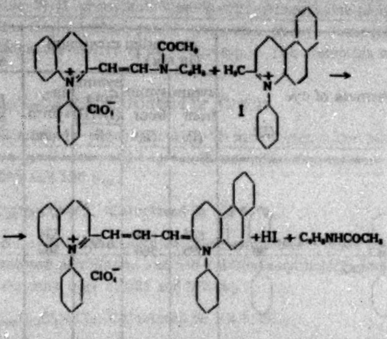
With the object of expanding the field of organic synthesis and of carrying out a more detailed investigation of the properties of the unsymmetrical molecules we undertook the synthesis of analogous intermediate products from quinoline derivatives containing aryl radicals on the hetero-nitrogen atom.

In this communication results of condensation of diphenylformamidine with N-phenylquinaldine perchlorate and N-phenylbenzoquinaldine iodide which proceeded as in the following scheme, are presented.





The substances obtained, N-phenyl-2-β-acetanilinovinylquinoline perchlorate (I) and N-phenyl-2-β-anilinovinyl-5,5-benzoquinoline iodide (II) were condensed with quaternary salts of quinaldine and benzthiazole derivatives with the formation of unsymmetrical trimethinecyanines.



It is known that unsymmetrical trimethinecyanine dyes differ markedly in properties from the corresponding symmetrical dyes. The asymmetry of the molecules brings about, in particular, a reduction in the strength of the electronic vibrations, as a direct consequence of which there is a marked reduction in the intensity of the molecular absorption of the unsymmetrical dyes in all cases without exception. It is of no less interest that the asymmetry of the molecules also has a strong effect on the superposition of the complex electronic movements, with the result that in the case of the unsymmetrical molecules, made up of heterocyclic bases differing in nature, the secondary shortwave absorption maxima are absent. On the other hand these maxima are always strongly expressed in the case of symmetrical quinoline and indolenine carbocyanine molecules.

The unsymmetrical dyes prepared by us, with quinoline perichromes at the ends of the polymethine chains have absorption maxima that show very little shift towards the shortwave part of the spectrum. This indicates that the nature of the secondary maxima is connected with the interaction of the electrons of the heterocyclic nucleus with the electron cloud of the main polymethine chromophore.

The carbocyanines synthesized from the intermediate products obtained are indicated in the Table.

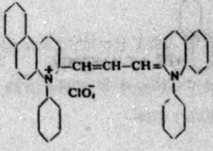
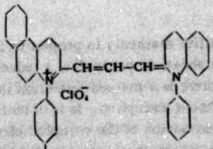
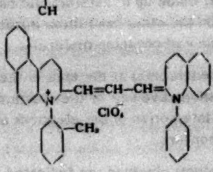
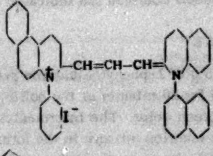
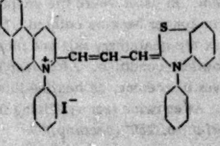
## EXPERIMENTAL

N-Phenyl-2-β-acetanilinovinylquinoline perchlorate. 0.5 g of 1-phenylquinaldine perchlorate, 0.4 g of diphenylformamidine and 3 ml of acetic anhydride were heated for 20 minutes at the boiling point of the reaction mixture, during which time the mixture acquired a bright green color. The intermediate product, phenylacetanilinovinylquinoline perchlorate, crystallized out from the reaction mixture in the form of dark green crystals which were filtered off and washed on the filter with alcohol. In cases where the product did not crystallize out the reaction mixture was treated with ether until the ether no longer became colored. The reaction product which comes out as a resin, was boiled with water for removal of the quaternary salt and rubbed with a rod in the presence of alcohol until it became converted to a solid, powdery condition. After recrystallizing from acetic acid 0.24g(33%) of product was obtained. This material dissolves in acetone, on heating in alcohol and acetic acid, and is not soluble in ether, benzene, toluene, chloroform. After twice recrystallizing from glacial acetic acid the intermediate product consisted of light green crystals of m. p. 255° (decomp.).

Found %: Cl 7.60; N 5.67, 6.11. $C_{25}H_{21}O_4N_2Cl$. Calculated %: Cl 7.62; N 6.02.

N-Phenyl-2-β-anilinovinyl-5,6-benzoquinoline iodide. A mixture of 0.5 g of 1-phenyl-5,6-benzoquinaldine iodide and 0.5 g of diphenylformamidine was ground vigorously in a mortar and melted on a water bath at 90° for 1 hour. The dark melt was treated with boiling water then with alcohol. By this means the quaternary salt, diphenylformamidine and possibly any symmetrical dye formed were dissolved in the alcohol and the intermediate product came out in the form of crystals, which after recrystallizing from a large quantity of alcohol melted at 300-301°. Yield 0.23 g (37.5%).

Found %: I 25.25, 25.08. $C_{27}H_{21}N_2I$. Calculated %: I 25.36.

| No. | Formula of dye | Absorption maximum (in mμ)* | | | | Shift from additivity | | M.p. |
|---|---|---|---|---|---|---|---|---|
| | (I) (II) | symm. from (I) | symm. from (II) | symm. from $\frac{(I)+(II)}{2}$ | un-symm. found | hypso-chromic | batho-chromic | |
| 1 |  | 645<br>595 | 614<br>566 | 629.5 | 624<br>582 | 5.5 | — | 257° (decomp.) |
| 2 |  | 642<br>592 | 614<br>566 | 628.0 | 625<br>580 | 3.0 | — | 251 (decomp.) |
| 3 |  | 644<br>600 | 614<br>566 | 629 | 623<br>578 | 6.0 | — | 276 (decomp.) |
| 4 |  | 645<br>595 | 618<br>574 | 631.5 | 625<br>580 | 6.5 | — | 279 (decomp.) |
| 5 |  | 645<br>595 | 558 | 601.5 | 596 | 5.5 | — | 220 (decomp.) |

**The intermediate products prepared and characterized, were condensed with salts of N-phenylquinaldine, N-phenylbenzoquinaldine, N-(p-tolyl)-benzoquinaldine, N-(α-naphthyl)-quinaldine and N-ethylbenzthiazole in a medium of pyridine with the addition of a small quantity of acetic anhydride. As a result of this the unsymmetrical carbocyanines were isolated.**

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*** In the absorption maxima the first number is the main maximum and the second number is the secondary shortwave maximum.**

(1-Phenyl-5,6-benzoquinoline-2)-(1-phenylquinoline-2)-trimethinecyanine perchlorate was obtained by condensation of 1-phenylacetanilinovinylquinoline perchlorate with 1-phenyl-benzoquinaldine iodide. The recrystallized, unsymmetrical carbocyanine melted at 257° (decomp.). The absorption maxima of the dye were at 624 and 582 mμ in ethanol.

Found %: Cl 5.85, 5.80. $C_{37}H_{27}O_4N_2Cl$. Calculated %: Cl 5.91.

(1-p-Tolyl-5,6-benzoquinoline-2)-(1-phenylquinoline-2)-trimethinecyanine perchlorate was synthesized from 1-phenylacetanilinoquinoline perchlorate and 1-p-tolylbenzoquinaldine iodide. M. p. 251° (decomp.). The absorption maxima were at 625 and 580 mμ.

Found %: Cl 5.54, 5.63. $C_{38}H_{27}O_4N_2Cl$. Calculated %: Cl 5.78.

(1-o-Tolyl-5,6-benzoquinoline-2)-(1-phenylquinoline-2)-trimethinecyanine perchlorate was synthesized from 1-phenylacetanilinovinylquinoline perchlorate and 1-o-tolylbenzoquinaldine iodide. The dye melted at 276° (decomp.). The absorption maxima were at 623 and 578 mμ.

Found %: Cl 5.63, 5.59. $C_{38}H_{27}O_4N_2Cl$. Calculated %: Cl 5.78.

(1-α-Naphthylquinoline-2)-(1-phenyl-5,6-benzoquinoline-2)-trimethinecyanine iodide was prepared by condensation of 1-phenylanilinovinylbenzoquinoline iodide with 1-α-naphthylquinaldine iodide. M. p. 279° (decomp.). The absorption maxima in ethanol were at 625 and 580 mμ.

Found %: I 18.52, 18.63. $C_{41}H_{29}N_2I$. Calculated %: I 18.76.

(1-Phenyl-5,6-benzoquinoline-2)-(3-ethylbenzthiazole-2) trimethinecyanine iodide was prepared by heating 1-phenylanilinovinylbenzoquinoline iodide with 2-methylbenzthiazole ethyliodide and also, as a control, from 2-β-acetanilinovinylbenzthiazole ethyliodide and 1-phenyl-5,6-benzoquinaldine iodide. Exactly the same dye was obtained in both cases. M. p. 220° (decomp.). The absorption maximum was at 596 mμ.

Found %: I 21.32, 21.46. $C_{31}H_{25}N_2I$. Calculated %: I 21.69.

## SUMMARY

1. The following new compounds, which are not described in the literature, have been synthesized: N-phenyl-2-β-acetanilinovinylquinoline perchlorate and N-phenyl-2-β-anilinovinyl-5,6-benzoquinoline iodide.

2. By condensation of the above-mentioned compounds with quaternary salts of heterocyclic bases 5 new, unsymmetrical carbocyanines have been prepared: a) (N-phenyl-5,6-benzoquinoline-2)-(N-phenylquinoline-2)-trimethinecyanine perchlorate; b) N-(p-tolyl-5,6-benzoquinoline-2)-(N-phenylquinoline-2)-trimethinecyanine perchlorate; c) N-(o-tolyl-5,6-benzoquinoline-2)-(N-phenylquinoline-2)-trimethinecyanine perchlorate; d) (N-phenyl-5,6-benzoquinoline-2)-(N-α-naphthylquinoline-2)-trimethinecyanine iodide; e) (N-phenyl-5,6-benzoquinoline-2)-(3-ethylbenzthiazole-2)-trimethinecyanine iodide.

## LITERATURE CITED

[1] T. Ogata, Pr. Imp. Acad. Tokyo 13, 325 (1937).

[2] U. S. Patent 2,071,898; 2,071,899 (1937); British Patent 466,269 (1937).

[3] A. I. Kiprianov and G. T. Piliugin, Sci. Reports Khar'kov State University 10, 104 (1937).

[4] L. G. S. Brooker, Rev. mod. Phys. 14, 275 (1942).

[5] G. T. Piliugin and Ia. Krainer, Proc. Acad. Sci. USSR 81, 609 (1951).

[6] G. T. Piliugin, Bull. Acad. Sci. USSR, Div.. Chem. Sci. 520 (1952).*

[7] T. Piliugin, Bull. Acad. Sci. USSR, Div. Chem. Sci. 736 (1952).*

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# RESEARCH IN THE FIELD OF SYNTHETIC DYESTUFFS

## XI. CONDENSATION OF SALTS OF N-ARYLQUINALDINE WITH NITROSO COMPOUNDS

G. T. Piliugin and S. V. Shinkorenko

By the interaction of primary aromatic amines and aldehydes, Schiff's bases or azomethine compounds are formed [1].

$$ArNH_2 + OCHAr' \rightleftarrows ArN{=}CHAr' + H_2O$$

It has been shown that azomethine compounds are also formed by condensing aromatic nitrosamines or nitrosophenols with compounds containing methylene or methyl groups with labile hydrogen atoms [2-4].

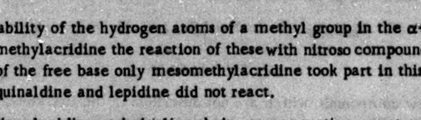
For this reaction sufficient lability of the hydrogen atom is ensured by the presence of such electrophilic groups as CN, $NO_2$, COOH, CHO etc., which by displacing the electron cloud weaken the bond between the hydrogen and carbon atoms [5].

In view of the relative lability of the hydrogen atoms of a methyl group in the α-position of quinaldine, 6-methylquinaldine and mesomethylacridine the reaction of these with nitroso compounds has been studied [6]; it was shown that in the form of the free base only mesomethylacridine took part in this reaction with the formation of an azomethine, while quinaldine and lepidine did not react.

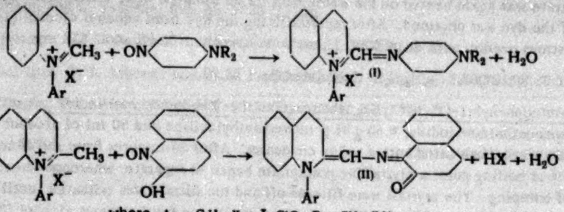
Haloalkylates of quinaldine, lepidine and picoline, being more reactive, react readily with nitroso compounds with the formation of azomethine compounds [7]. The azomethine compounds prepared by condensation of quaternary salts of benzthiazole and indolenine with nitroso compounds have been studied [8]. It was shown that the azomethines are more deeply colored than the corresponding styryl derivatives.

The azomethine compounds are of definite scientific interest because they are deeply colored and on heating with dilute acids can be split with the formation of aldehydes and primary amines. Furthermore the azomethine dyes are used in color photography by use of multilayer films with color development of the image in depth, in the form of dyes [9].

Thus bearing in mind the considerable importance of the azomethine compounds it was of interest to study the reaction of some new N-arylquinaldine quaternary salts, prepared by us, with aromatic nitroso compounds. In consequence of the presence in these onium compounds of electrophilic radicals on the hetero nitrogen atom the hydrogen atoms of the methyl group in the α-position are more labile than in the haloalkylates of quinaldine and 2-methylbenzthiazole [10].

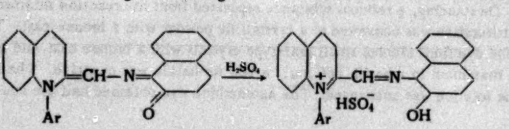


It was assumed that the reaction in question should take place relatively easily. As a result of this reaction it is possible to form azomethine coloring materials that have not previously been described in the literature. We carried out the condensation of N-phenylquinaldine perchlorate and N-phenyl-5,6-benzoquinaldine iodide with p-nitrosodimethylaniline and p-nitrosodiethylaniline, and also with α-nitroso-β-naphthol. The reaction proceeded according to the scheme:



where $Ar = C_6H_5$; $X = I$, $ClO_4$; $R = CH_3$, $C_2H_5$.

The absorption maxima of these salt-type azomethines are in a longer wavelength part of the spectrum than those of the corresponding styryl derivatives and in a shorter wavelength part in comparison with the carbocyanines. By condensation of the salts with nitroso-β-naphthol, hydroxyazomethine dye bases were obtained, this being confirmed by analysis and by the identity of the absorption spectrum curves in neutral and alkaline solution. On converting the dyes to the salt form by the addition of sulfuric or hydrochloric acids the color is increased in consequence of the lowering of the energetic level of the molecule and the change in structure.



Hydroxyazomethines change color depending on the solvent, i.e., they possess the property of solvatochromism. The condensation of nitroso compounds with N-arylquinaldine salts goes very smoothly without the use of condensing agents, which indicates the high reactivity of the methyl group.

## EXPERIMENTAL

4-Dimethylaminophenyl-1-(1'-phenylquinoline-2'-azomethine) perchlorate. A mixture of 1.5 g of N-phenylquinaldine perchlorate, 0.7 g of p-nitrosodimethylaniline and 30 ml alcohol was heated on the water bath in a flask fitted with a reflux condenser. About 1.5 hours after the reaction mixture reached boiling point a crystalline precipitate began to separate in the form of small needles with a green luster. Further heating was accompanied by bumping, hence heating was discontinued after 15 minutes. On the following day the dye precipitated was filtered off and washed with alcohol. The filtrate was again heated up to the point of separation of dye. In all 1.45 g (68.4%) of dye was obtained. The dye was recrystallized from alcohol and then from aqueous alcohol (1:1). The melting point of the substance was 251-252°. Absorption maximum in ethanol, 587 mμ. The absorption curve was plotted on a recording spectrophotometer SF-2M.

Found %: Cl 8.04, 7.78. $C_{24}H_{22}O_4N_3Cl$. Calculated %: Cl 7.84.

4-Diethylaminophenyl-1-(1'-phenylquinoline-2'-azomethine) perchlorate. 1.5 g of N-phenylquinaldine perchlorate, 0.84 g of p-nitrosodiethylaniline and 30 ml of alcohol were placed in a flask fitted with a reflux condenser and heated on a boiling water bath for 1 hour 40 minutes. On the following day the dye was filtered off and washed with alcohol, and the filtrate was heated again for 20 minutes; an additional quantity of material was thus obtained. Yield 1.4 g (62.2%). The dye was crystallized from alcohol and then from aqueous alcohol (2:3). Long needles with a green luster. M. p. 252°. Absorption maximum, 587 mμ.

Found %: Cl 7.67, 7.42. $C_{26}H_{26}O_4N_3Cl$. Calculated %: Cl 7.38.

4-Dimethylaminophenyl-1-(1'-phenyl-5,6-benzoquinoline-2'-azomethine) iodide. 0.57 g of p-nitrosodimethylaniline, 1.5 g of N-phenyl-5,6-benzoquinaldine iodide and 40 ml of alcohol were placed in a flask fitted with a reflux condenser and heated on a boiling water bath for 30 minutes, after which the dye began to separate in the form of small needles with a bronze luster. After about 10 hours the precipitated dye was filtered and the filtrate was again heated on the water bath for 20 minutes, after which more dye precipitated. 1.02 g (51.2%) of the dye was obtained. After recrystallizing the dye from aqueous alcohol (1:1) it consisted of long, green lustrous needles with m. p. 273°. Absorption maximum in ethanol, 573 mμ.

Found %: I 23.90, 23.67. $C_{28}H_{24}N_3I$. Calculated %: I 23.97.

4-Diethylaminophenyl-1-(1'-phenyl-5,6-benzoquinoline-2'-azomethine) iodide. A mixture of 1.5 g of N-phenyl-5,6-benzoquinaldine iodide, 0.65 g of p-nitrosodiethylaniline and 30 ml of alcohol were heated on a boiling water bath in a flask fitted with a reflux condenser. After 30 minutes from the time that the reaction mixture reached boiling point a crystalline precipitate began to separate, whereupon heating was discontinued because of bumping. The crystals were filtered off and the filtrate was reheated until crystals again began to separate. Yield of dye 0.95 g (45.2%). After recrystallizing from aqueous alcohol (3:2) the dye was obtained as small needles with a green luster and m. p. 276°. Absorption maximum in ethanol, 574 mμ.

Found %: I 22.79, 22.88. $C_{30}H_{28}N_3I$. Calculated %: I 22.76.

2-Oxonaphthyl-1-(1'-phenylquinoline-2)-azomethine. The directions of Kiprianov and Fridman [8] were taken as the basis of the synthesis of this compound. A mixture of 0.5 g of N-phenylquinaldine perchlorate and 0.25 g of α-nitroso-β-naphthol was dissolved by heating in 5 ml alcohol. To the hot alcoholic solution were added 2-3 drops of piperidine whereupon the color of the reaction mixture changed immediately from yellow-brown to blue-green. On standing, a resinous substance separated from the reaction mixture, which on addition of 5 ml of water and trituration was converted to a crystalline powder with a bronze cast. Yield 0.54 g (91.5%). After recrystallizing the dye from alcohol small leaf-type crystals with a bronze cast and m. p. 167-168° were obtained. Absorption maximum in ethanol, 660 mμ. A test for halide was negative. The absorption maximum in neutral and alkaline solution was unchanged. The azomethine dye obtained had the structure of the free base (II).

2-Oxonaphthyl-1-(1'-phenyl-5,6-benzoquinoline-2'-)-azomethine. 0.5 g of N-phenyl-5,6-benzoquinaldine iodide and 0.22 g of α-nitroso-β-naphthol were dissolved on heating in 5 ml alcohol; 2-3 drops of piperidine were added whereupon the color of the solution changed immediately, becoming blue-green. 5 ml of water was added to the reaction mixture and on standing the dye separated in the form of a dark blue crystalline powder with a bronze cast. The dye was recrystallized from an acetone-water mixture (10:1); long needles with a bronze luster and m. p. 198-200°. Yield of product, 0.44 g (83%). Absorption maximum in ethanol, 659 mμ. The analytical data indicate that this azomethine dye does not have a salt-type structure.

Found %: N 6.55, 6.51. $C_{30}H_{20}ON_2$. Calculated %: N 6.59.

## SUMMARY

1. By condensing salts of N-arylquinaldines, containing an active methyl group in the α-position, with nitrosamines, four azomethine dyes not described in the literature, have been obtained: a) 4-dimethylaminophenyl-1-(1'-phenylquinoline-2'-azomethine) perchlorate; b) 4-diethylaminophenyl-1-(1'-phenylquinoline-2'-azomethine) perchlorate; c) 4-dimethylaminophenyl-1-(1'-phenyl-5,6-benzoquinoline-2'-azomethine) iodide; and d) 4-diethylaminophenyl-1-(1'-phenyl-5,6-benzoquinoline-2'-azomethine) iodide.

2. Two azomethine dye bases have been prepared by condensing salts of N-arylquinaldines with α-nitroso-β-naphthol: a) 2-oxonaphthyl-1-(1'-phenylquinoline-2)-azomethine and b) 2-oxonaphthyl-1-(1'-phenyl-5,6-benzoquinoline-2')-azomethine.

## LITERATURE CITED

[1] F. Sachs and N. Lewin, Ber. 35, 3573 (1902).

[2] F. Sachs, Ber. 33, 959 (1900).

[3] F. Sachs and E. Bry, Ber. 34, 118 (1901).

[4] F. Sachs and R. Kempf, Ber. 35, 1224 (1902); Ber. 35, 2704 (1902).

[5] F. Sachs and M. Goldmann, Ber. 35, 3319 (1902).

[6] A. E. Porai-Koshits, Iu. Aushkap and N. Amsler, J. Russ. Chem. Soc. 42, 518 (1910).

[7] A. Kaufmann and L. Vallette, Ber. 45, 1738 (1912).

[8] A. I. Kiprianov and S. G. Fridman, Ukrainian Chem. J. 14, 50 (1948).

[9] V. S. Chel'tsov, G. I. Arbuzov and A. N. Iordanskii, Prog. Chem. 14, 324 (1945).

[10] G. T. Piliugin, Bull. Acad. Sci. USSR, Div. Chem. Sci. 353 (1952).*

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* Original Russian pagination. See C. B. Translation.

# THE REDUCTION OF THE BISULFITE COMPOUND OF 1-NAPHTHOL

## I. 1,2-DIHYDRONAPHTHALENE-2-SULFONIC ACID

S. V. Bogdanov

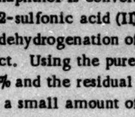
It has been reported [1] that the bisulfite compound of 1-naphthol behaves as a ketone with respect to hydroxylamine and semicarbazide, being converted to the oxime and semicarbazone of the bisulfite compound. On these grounds the structure 1-oxo-1,2,3,4-tetrahydronaphthalene-3-sulfonic acid (I) has been proposed for this compound.

According to the literature [2,3] reduction of 1-oxo-1,2,3,4-tetrahydronaphthalene leads to 1-hydroxy-1,2,3,4-tetrahydronaphthalene and 1,1'-dihydroxy-1,1'-ditetralin. It seemed of interest to follow the reduction of the bisulfite compound of 1-naphthol also.

Experiment showed that by the action of zinc and dilute acetic acid in the presence of copper sulfate the bisulfite compound of 1-naphthol is converted to a mixture of reduction products from which the sodium salt of 1,2-dihydronaphthalene-2-sulfonic acid (II) was isolated. The formation of the dihydronaphthalenesulfonic acid (II) can be explained by dehydrogenation of 1-hydroxy—1,2,3,4-tetrahydronaphthalene-3-sulfonic acid formed as an intermediate product. Using the pure bisulfite compound under the above conditions the yield of the sulfonic acid (II) was 52-55% and the residual bisulfite compound was 6%. With impure bisulfite compound containing mineral salts and a small amount of 1-naphthol sulfonic acids as impurities the reaction did not proceed so well.

The sodium salt of dihydronaphthalenesulfonic acid is stable under normal conditions but on heating with dilute caustic alkalis and with mineral acids it behaves as a" bisulfite compound of naphthalene" and breaks down into naphthalene and sulfurous acid; under reducing conditions the naphthol bisulfite compound is unchanged. In contrast to the naphthol bisulfite compound it reacts with bromine in an aqueous medium and is stable under the conditions for the iodometric analysis of a bisulfite compound [4]. The content of the sulfonic acid (II) in the solution of the bisulfite compound reduction products was determined by the bromide-bromate method (1 molecule of sulfonic acid requires 2 atoms of bromine), and the residual bisulfite compound by its decomposition with alkali and titration of the sulfurous acid with iodine. The other bisulfite compound reduction products showed no noticeable effect on the analytical results under the conditions chosen.

The sulfonic acid (II) with bromine-water adds on a molecule of hypobromous acid and is converted to 4-hydroxy-3-bromo-1,2,3,4-tetrahydronaphthalene-2-sulfonic acid (III). This addition of hypobromous acid to (II) corresponds to the conversion of 1,2-dihydronaphthalene to 1-hydroxy-2-chloro-1,2,3,4-tetrahydronaphthalene by the action of hypochlorous acid [2].



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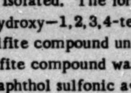
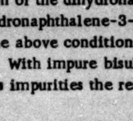


(II)



(III)

The bromine derivative (III) forms a mixture of naphthalene and 2-bromonaphthalene with 40% sulfuric acid and, with 10% sodium hydroxide, converts it to naphthalene-2-sulfonic acid. These transformations indicate the structures of the bromine derivative (III) and the dihydronaphthalenesulfonic acid (II), and hence they confirm structure (I) for the bisulfite compound of 1-naphthol.

## EXPERIMENTAL

The bisulfite compound of 1-naphthol (I) used in the reduction experiments was prepared from 1-naphthol and was recrystallized from aqueous alcohol. The presence of 1-naphthol sulfonic acids in the impure bisulfite compound was shown by converting them to the corresponding nitroso compounds. The aqueous solution of the residue obtained by evaporating down the filtrate from recrystallization of the bisulfite compound was treated with alkali, acidified and the 1-naphthol extracted with ether. On addition of nitrite to the aqueous part 4-nitroso-1-naphthol-2-sulfonic acid precipitated, and was characterized by the absence of a coloration with ferrous sulfate and by conversion on heating with nitric acid to 2,4-dinitronaphthol with m. p. 138-139° (decomp.). The filtrate from this nitroso compound gave a green coloration with ferrous sulfate indicating the presence of 2-nitroso-1-naphthol-4-sulfonic acid. 1-Naphthol-4-sulfonic acid was also found in the filtrate from the salted-out bisulfite compound. After removal of residual bisulfite compound it was converted to 2-nitroso-1-naphthol-4-sulfonic acid which gave an intense green coloration with ferrous sulfate, was converted to 2,4-dinitro-1-naphthol by the action of nitric acid and on reduction gave 2-amino-1-naphthol-4-sulfonic acid. The latter was characterized by conversion to 2-diazo-1-naphthol-4-sulfonic acid and to 1,2-naphthoquinone-4-sulfonic acid. Sulfonation of the naphthol during the preparation of the bisulfite compound probably arises from the simultaneous action of sulfurous acid and air [5].

1,2-Dihydronaphthalene-2-sulfonic acid (II). To a solution of 21.1 g of 94.19% bisulfite compound (I) and 2 g of copper sulfate in 200 ml of water at 50°, acidified with 40 ml of 98% acetic acid, 21 g of zinc dust was added over a period of half an hour and the mixture was stirred for 4 hours at 90-92°. The unreacted zinc (10.7 g) was filtered off and the filtrate was made up to 500 ml with water. For determination of the yield of the sulfonic acid (II), to 25 ml of the solution was added 175 ml of water, 10 ml of hydrochloric acid and 10 ml of a 20% potassium bromide solution, and the mixture was titrated with 0.2N potassium bromate to reaction with starch-iodine paper. At this point the previously colorless solution acquires a faint yellow color. For determination of residual bisulfite compound another 25 ml of the solution was made alkaline with 25 ml of 37% sodium hydroxide; after 15 minutes it was diluted with 1.5 liters of water, acidified with 40 ml of hydrochloric acid and titrated with 0.1N iodine. The yield of sodium salt of the sulfonic acid (II) was 10.22 g (55%) and the residual bisulfite compound was 1.26 g (6.3%). To the remaining solution, after evaporating down to 180 ml, 36 g sodium chloride was added and the sodium salt of the sulfonic acid (II) that separated was filtered off and washed with alcohol. Yield 8.9 g (78.6%).

In 18 similar experiments the yield of the sulfonic acid (II) in solution was 52-55%. From all the solutions, corresponding to 1.36 moles bisulfite compound, 163.5 g (39.6%) of 76.5% sodium salt of sulfonic acid (II) was isolated.

On reduction of the bisulfite compound in the absence of copper sulfate, solution of the zinc was strongly retarded and the yield of the sulfonic acid (II) was poor. The use of impure bisulfite compound resulted in rapid and almost complete solution of the zinc, a fall in the yield of the sulfonic acid (II) to 20-30% and an increase in the unreacted bisulfite compound.

In order to test the stability of the sulfonic acid (II) under reducing conditions 4.92 g of 94.4% sodium salt (II) was treated as above with zinc and acetic acid in the presence of copper sulfate for 7.5 hours. In the filtrate after removal of residual zinc 98.5% of the original material was found by bromate titration. From the main part of the filtrate after concentrating and salting out, 4.12 g, corresponding to 0.018 mole of sulfonic acid taken, of 94.04% sodium salt was isolated. Yield 92.7%.

The sodium salt of dihydronaphthalenesulfonic acid (II) crystallizes in colorless, thick, tetragonal plates (from aqueous alcohol or water), dissolving readily in water and with difficulty in alcohol; it contains no water of crystallization.

Found %: C 51.42, 51.50; H 4.13, 4.10; Na 9.71, 9.86. M (bromometric method) 233.6, 234.3. $C_{10}H_9O_3SNa$. Calculated %: C 51.70; H 3.90; Na 9.90. M 232.2.

Decomposition of sulfonic acid (II). A mixture of 1.1 g of 91.86% sodium salt (II) and 50 g of 9.7% sodium hydroxide was refluxed for 6 hours. The naphthalene formed was washed out of the condenser with hot water and was filtered off after cooling the mixture. Yield 0.52 g (93.4%), m. p. 80°. The filtrate evolved sulfur dioxide on acidification.

On boiling a mixture of 1 g of sodium salt (II) and 100 g of a 15% sodium carbonate solution for 8 hours only traces of naphthalene were obtained; 0.73 g of the original material was isolated.

Refluxing a solution of 1 g of the sodium salt in 100 ml of 5% hydrochloric acid for 6.5 hours yielded 0.15 g of naphthalene.

4-Hydroxy-3-bromo-1,2,3,4-tetrahydronaphthalene-2-sulfonic acid (III). A solution of 24.54 g of 94.62% sodium salt (II) in 125 ml of water was cooled rapidly and to the resulting suspension at 6° saturated bromine-water at 5-10° was added over a period of 1 hour up to the appearance of a stable reaction with starch-iodine paper (446 ml). 190 g of anhydrous sodium acetate was added to the solution at 20-25° and the sodium salt of (III) that separated was filtered and washed with alcohol. Yield 32.4 g.

The sodium salt of (III) crystallizes in tetragonal and hexagonal plates (from aqueous alcohol), dissolving readily in water and with difficulty in alcohol. Water of crystallization is lost slowly at ordinary temperatures over phosphorus pentoxide; at 100-110° it decomposes.

Found %: $H_2O$ 9.82; C 32.80, 32.73; H 3.63, 3.81; Br 21.66, 21.52; Na 6.13, 6.08. $C_{10}H_{10}O_4BrSNa \cdot 2H_2O$. Calculated %: $H_2O$ 9.87; C 32.89; H 3.86; Br 21.89; Na 6.30.

2-Bromonaphthalene. A mixture of 8 g of the bromo derivative (III) and 150 ml of 40% sulfuric acid was refluxed for 2 hours and the naphthalene and bromonaphthalene formed were distilled out with steam; 1.15 g of material of m. p. 50-53° and 1.65 g of m. p. 46-47° was obtained. To a solution of 1.45 g of the second fraction in 15 ml of alcohol a solution of 1.7 g of picric acid in 17 ml of alcohol was added and the precipitate that separated was filtered off after 24 hours (0.9 g, m. p. 100-137°). The filtrate was evaporated to dryness, the residue (2.1 g, m. p. 79.5-81°) was treated with sodium hydroxide and impure bromonaphthalene was steam-distilled out; 0.1 g of product of m. p. 46-47° and 0.97 g of m. p. 51-52° were obtained. The substance of m. p. 51-52° was recrystallized from alcohol in the form of plates of m. p. 54-55° that gave no melting point depression with 2-bromonaphthalene (m. p. 55°).

Naphthalene-2-sulfonic acid. To 150 ml of 10% sodium hydroxide at 95°, 5 g of the bromo derivative (III) was added in one lot and the solution was refluxed for 2 hours. The mixture was acidified with hydrochloric acid and evaporated to 110 ml. The precipitate that separated was filtered off and washed with alcohol. Yield 1.67 g (formation of naphthalene and sulfite was not observed).

The sodium salt consisted of tetragonal and hexagonal plates (from aqueous alcohol).

Found %: C 52.17, 52.18; H 2.90, 2.96; S 13.81, 13.72; $C_{10}H_7O_2SNa$. Calculated %: C 52.17; H 3.07; S 13.93.

The sulfonylchloride consisted of tetragonal and hexagonal plates (from acetic acid), m. p. 75.5-76.5°; it gave no melting point depression with naphthalene-2-sulfonylchloride (m. p. 75-76°).

The sulfonamide consisted of tetragonal and hexagonal plates (from alcohol) m. p. 215.5-216.5°; it gave no melting point depression with naphthalene-2-sulfonamide (m. p. 216-216.5°).

## SUMMARY

1. On reacting 1-naphthol with bisulfite, 1,2- and 1,4-naphtholsulfonic acids are formed in addition to the bisulfite compound.

2. By reduction of the bisulfite compound of 1-naphthol with zinc and acetic acid 1,2-dihydronaphthalene-2-sulfonic acid is obtained, together with other products.

3. 1,2-Dihydronaphthalene-2-sulfonic acid breaks down with alkalis and mineral acids to naphthalene and sulfurous acid, and is converted to 4-hydroxy-3-bromo-1,2,3,4-tetrahydronaphthalene-2-sulfonic acid by the action of bromine-water.

4. 4-Hydroxy-3-bromo-1,2,3,4-tetrahydronaphthalene-2-sulfonic acid gives naphthalene and 2-bromonaphthalene in acidic media and naphthalene-2-sulfonic acid in alkaline media.

5. The formation of 1,2-dihydronaphthalene-2-sulfonic acid on reduction of the bisulfite compound of 1-naphthol confirms the structure of the latter as 1-oxo-1,2,3,4-tetrahydronaphthalene-3-sulfonic acid (I).

## LITERATURE CITED

[1] S. Bogdanov and N. Karandasheva, J. Gen. Chem. 26, 3365 (1956).*

[2] F. Straus and A. Rohrbacher, Ber. 54, 40 (1921).

[3] G. Schroeter, Ber. 58, 713 (1925).

[4] N. Karandasheva and S. Bogdanov, J. Gen. Chem. 25, 1152 (1955).*

[5] S. Bogdanov, J. Gen. Chem. 15, 967 (1945).

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# THE REDUCTION OF THE BISULFITE COMPOUND OF 1-NAPHTHOL AND ITS OXIME II

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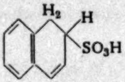
It was recently reported [1] that by reduction of the bisulfite compound of 1-naphthol with zinc and acetic acid a mixture of reaction products is formed, from which 1,2-dihydronaphthalene-2-sulfonic acid (I) was isolated. The precipitate that separated from the solution by the addition of sodium chloride contained 76.5% of the sodium salt of (I) and a considerable quantity of the sodium salt of a sulfonic acid that was inert to iodine and bromine-water and stable to alkalis and acids. It was separated from the main constituent (I) by fractional crystallization from water and boiling with 10% sodium hydroxide. From its composition and properties this compound is a tetrahydronaphthalenesulfonic acid and by dehydrogenation with sulfur it is converted to naphthalene-2-sulfonic acid; hence it can be surmised that it is the salt of 1,2,3,4-tetrahydronaphthalene-2-sulfonic acid (II). Judging by the composition of the salted out mixture of sulfonic acids the yield of the tetrahydronaphthalenesulfonic acid exceeds 11%. Its formation probably results from direct reduction of the bisulfite compound since compound (I) is stable to the action of zinc and acetic acid.



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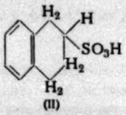
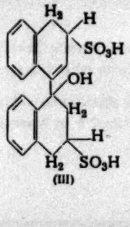


(II)

From the filtrate from the salted out mixture of salts (I) and (II) yet another substance was isolated in very small yield. On heating with 10% sodium hydroxide or 40% sulfuric acid it decomposes to 1,1'-dinaphthyl and sulfurous acid, and it reacts with bromine-water. This same compound was obtained in somewhat better yield (7%) by the reduction of the bisulfite compound of 1-naphthol with zinc and hydrochloric acid. The composition of this compound corresponds to the formula of the sodium salt of (1-hydroxy-1,2,3,4-tetrahydro)-(3',4'-dihydro)-1,1'-dinaphthyl-3,3'-disulfonic acid (III). Its formation probably proceeds through the corresponding pinacone.

The fission of (III) into 1,1'-dinaphthyl and sulfurous acid by the action of sodium hydroxide is effected in two stages. In the first stage, which proceeds fairly rapidly, the sodium salt of the monosulfonic acid, which is difficultly soluble in water, is formed; the second, slower stage leads to the dinaphthyl. An intermediate substance formed reacts with bromine-water and its composition corresponds to the sodium salt of (1-hydroxy-1,2,3,4-tetrahydro)-1,1'-dinaphthyl-3-sulfonic acid (IV).



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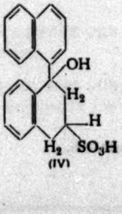

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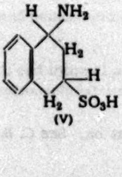

(V)

Reduction of 1,2,3,4-tetrahydronaphthalene-1-oxime with sodium in alcohol yields 1-amino-1,2,3,4-tetrahydronaphthalene [2]. It seemed interesting to carry out the reduction of the oxime of the bisulfite compound of 1-naphthol also. In this case, using zinc and dilute acetic acid in the presence of copper, a substance was obtained in 55% yield that was stable to alkalis and acids and the composition of which corresponded to 1-amino-1,2,3,4-tetrahydronaphthalene-3-sulfonic acid (V). As side products, we detected the bisulfite compound of 1-naphthol, formed evidently by hydrolysis of the oxime group, and its reduction product – 1,2-dihydronaphthalene-2-sulfonic acid (I).

The course of the reduction of the bisulfite compound of 1-naphthol and its oxime, leading respectively to a mixture of (I), (II) and (III) and to (V) does not differ in principle from that of the reduction of 1-oxo-1,2,3,4-tetrahydronaphthalene and its oxime and confirms the structural formulas of the bisulfite compound of 1-naphthol and its oxime proposed previously [3].

## EXPERIMENTAL

1,2,3,4-Tetrahydronaphthalene-2-sulfonic acid (II). A suspension of 22.7 g of a mixture of the sodium salts of sulfonic acids (II) and (I) [obtained by evaporating the filtrate from the first crystallization of the sodium salt of (I) and containing 29% of (I)] in 285 ml of 9.6% sodium hydroxide was refluxed for 7.5 hours; the bulk of the naphthalene formed from (I) was deposited in the reflux condenser. The mixture was diluted with water, acidified with hydrochloric acid and the solution evaporated to 225 ml. The precipitate was filtered off and washed with alcohol; yield 13.65 g. The product contained 3.6% of sulfonic acid (I) and was purified by recrystallizing from water.

The sodium salt of (II) consists of long, colorless tetragonal plates, dissolving readily in water and with difficulty in alcohol. It does not react with bromine or iodine in an acidic aqueous medium. It loses water of crystallization at 100-105°.

Found %: $H_2O$ 7.05, 7.19. $C_{10}H_{11}O_3SNa \cdot H_2O$. Calculated %: $H_2O$ 7.14. Found %: C 50.93, 51.02; H 4.65, 4.79; Na 9.66, 9.56. $C_{10}H_{11}O_3SNa$. Calculated % C 51.26; H 4.73; Na 9.82.

The sulfonyl chloride consists of long plates (from acetic acid), m. p. 72-73°; a mixture with naphthalene-2-sulfonyl chloride (m. p. 75-76°) melted at 50-53°.

Found %: Cl 14.99, 15.33. M (in benzene) 214.8, 221.7. $C_{10}H_{11}O_2ClS$. Calculated %: Cl 15.37. M 230.7.

The sulfonamide consists of tetragonal and hexagonal, thick plates (from alcohol), m. p. 142-143°.

Found %: N 6.59, 6.61. $C_{10}H_{13}O_2NS$. Calculated %: N 6.63.

Naphthalene-2-sulfonic acid. A mixture of 2.1 g of dry sodium salt of (III) and 1.15 g of sulfur was heated in a test tube in a metal bath, with frequent stirring, at 250° until evolution of hydrogen sulfide ceased (2.5 hours). The ground melt was extracted with hot water, the solution treated with charcoal, and evaporated to dryness. The residue was converted to the sulfonyl chloride and then to the sulfonamide.

The sulfonamide consists of tetragonal plates (from alcohol), m. p. 215.5-216.5° and gives no melting point depression with naphthalene-2-sulfonamide.

(1-Hydroxy-1,2,3,4-tetrahydro)-(3',4'-dihydro)-1,1'-dinaphthyl-3,3'-disulfonic acid (III). 1) The filtrate from the salted out mixture of sodium salts of (I) and (II), after the separation of zinc with sodium carbonate, was acidified with hydrochloric acid and evaporated on a water bath. The turbid liquid was decanted from the sodium chloride, deposited, and cooled. The precipitate formed was filtered off, the filtrate stirred with the sodium chloride deposited on evaporating, the liquid containing the suspended reduction products was decanted off, re-evaporated, etc. The reduction products and the naphthol bisulfite compound were contained in the residue filtered out. For the separation of (III) the mixture was crystallized from water; a fraction containing a considerable amount of (I) was discarded. From the total filtrates, corresponding to 1.36 moles of initial bisulfite compound 8.6 g of pure sodium salt of (III), 6.4 g of a mixture of the latter with the sodium salt of (II) and 9.2 g of a mixture of all three reduction products together with unchanged bisulfite compound, were isolated.

2) 31.5 g of zinc dust was added over a period of half an hour to a solution of 33.27 g of 89.5% bisulfite compound of 1-naphthol in 300 ml of water, acidified with 90 ml of 34.4% hydrochloric acid at 20-35°, and the

mixture was maintained for 4 hours at 50°. Evolution of hydrogen sulfide occurred during the reaction. Residual bisulfite compound, determined iodometrically, was 0.96-1.2%. In order to isolate the sodium salt of (III) the solution of reduction products, obtained from 0.24 moles of bisulfite compound, after precipitating the zinc with sodium carbonate and acidifying with hydrochloric acid, was evaporated to 520 ml and cooled. The precipitate (colorless needles and prisms) was filtered off and washed with alcohol; yield 9.4 g (7.7%).

The sodium salt consists of long, colorless prisms (from water), dissolving readily in water and with difficulty in alcohol. In contrast to (I), (II) and the original bisulfite compound, it forms a precipitate with silver nitrate (long, colorless prisms, soluble on heating). Under the conditions for the analysis of the bisulfite compound it does not take up iodine. It reacts with bromine in an acidic medium. Under the conditions for the determination of (I), particularly toward the end, the reaction goes very slowly and the solution immediately acquires a yellow color. A little more than 4 atoms of bromine are taken up by 1 molecule of the substance. It loses water of crystallization at 100°.

Found %: $H_2O$ 5.65, 5.56. $C_{20}H_{18}O_7S_2Na_2 \cdot 1.5H_2O$. Calculated %: $H_2O$ 5.32. Found %: C 49.43, 49.51; H 4.01, 3.91; S 13.23, 13.57; Na 9.44, 9.41. $C_{20}H_{18}O_7S_2Na_2$. Calculated %: C 50.00; H 3.78; S 13.35; Na 9.58.

(1-Hydroxy-1,2,3,4-tetrahydro)-1,1'-dinaphthyl-3-sulfonic acid (IV) and 1,1'-dinaphthyl. A mixture of 5 g of the sodium salt of (III) and 350 ml of 9.8% sodium hydroxide was refluxed for 2 hours; after 45 minutes an almost transparent solution was formed but immediately the reaction products began to separate. The mixture was diluted with water, the precipitate filtered off and washed with water; the weight of reaction products was 3.75 g. On acidification the filtrate evolved sulfur dioxide. For separation of the sodium salt of (IV) and 1,1'-dinaphthyl, 7.5 g of the mixture was twice extracted with boiling water (200 ml each time). Sodium chloride was added to the filtrate and the sodium salt of (IV) that precipitated was filtered off and washed with water. The yield of dinaphthyl was 0.6 g and the sodium salt of (IV) – 6.68 g.

The sodium salt of (IV) consists of long, hexagonal plates (from water), dissolving with difficulty in cold water and considerably more readily in hot; it dissolves well in alcohol. Under the conditions for the determination of (I) it requires more than two atoms of bromine; the reaction goes very slowly toward the end and the solution acquires a brownish-yellow color. It loses water of crystallization over phosphorus pentoxide at room temperature.

Found %: $H_2O$ 11.38, 11.49. $C_{20}H_{17}O_4SNa \cdot 2.5H_2O$. Calculated %: $H_2O$ 10.69. Found %: C 64.45, 64.48; H 5.14, 4.64; Na 6.17, 6.00. $C_{20}H_{17}O_4SNa$. Calculated %: C63.81; H 4.55; Na 6.11.

1,1'-Dinaphthyl. 1) A suspension of 2 g of the sodium salt of (III) in 100 ml of 40% sulfuric acid was refluxed for 3 hours. The mixture was diluted with water and the dinaphthyl was filtered off and washed with water; yield 0.9 g.

2) A mixture of 1 g of the sodium salt of (IV) and 70 ml of 9.8% sodium hydroxide was refluxed for 15 hours. The mixture was diluted with water and the dinaphthyl was filtered off and washed with boiling water to remove unchanged (IV); yield 0.45 g. On acidifying the filtrate sulfur dioxide was evolved. On substituting sodium hydroxide by 40% sulfuric acid the reaction proceeds at a considerably faster rate.

Thick tetragonal and hexagonal colorless plates or short prisms (from alcohol), m. p. 159.5-160°.

Found %: C 94.36, 94.04; H 5.58, 5.49. M (in benzene) 241.2, 232.7. $C_{20}H_{14}$. Calculated %: C 94.48; H 5.55, M 254.3.

1-Amino-1,2,3,4-tetrahydronaphthalene-3-sulfonic acid (V). 10 g of zinc powder was added to a solution of 10.52 g of the oxime of the bisulfite compound of 1-naphthol and 1 g of copper sulfate in 100 ml of water acidified with 20 ml of 98% acetic acid, over a period of half an hour at 20-50°, and the mixture was maintained at 90° for 2 hours and then at 5° for 2 hours. The mixture of zinc and (V) was filtered off and (V) was extracted with a boiling sodium carbonate solution and precipitated with hydrochloric acid. A further quantity of (V) was isolated by evaporation of the main filtrate to 70 ml; its total yield was 5 g (55%). After further evaporation of the filtrate to 40 ml zinc acetate was filtered off and addition of sodium chloride to the filtrate yielded 0.5 g of the sodium salt of (I). The final filtrate contained (I) and the bisulfite compound of 1-naphthol.

Colorless, long plates and prisms, dissolving with difficulty in water and alcohol, does not contain water of crystallization. Remains unchanged on boiling with 9.7% sodium hydroxide and with 40% sulfuric acid.

The sodium salt is very readily soluble in water but is stable only in the presence of excess alkali.

Found %: C 52.78, 52.61; H 5.85, 5.74; N 6.15, 6.32; S 14.10, 14.32. $C_{10}H_{13}O_3NS$. Calculated %: C 52.84; H 5.77; N 6.16; S 14.10.

Benzoyl derivative. This was prepared from (V) and benzoyl chloride in the presence of sodium hydroxide. The sodium salt consists of colorless, long hexagonal, thin plates (from aqueous alcohol); dissolves readily in water and with difficulty in alcohol. Gives a precipitate with silver nitrate (colorless, long, hexagonal plates) soluble on heating. Loses water of crystallization at 100°.

Found %: $H_2O$ 9.32, 9.31. $C_{17}H_{16}O_4NSNa \cdot 2H_2O$. Calculated %: $H_2O$ 9.25. Found %: N 3.87, 3.83; Na 6.34, 6.33. $C_{17}H_{16}O_4NSNa$. Calculated %: N 3.96; Na 6.51.

## SUMMARY

1. On reduction of the bisulfite compound of 1-naphthol with zinc and acetic acid, in addition to 1,2-dihydronaphthalene-2-sulfonic acid (I), 1,2,3,4-tetrahydronaphthalene-3-sulfonic acid (II) and (1-hydroxy-1,2,3,4-tetrahydro)-(3',4'-dihydro)-1,1'-dinaphthyl-3,3'-disulfonic acid (III) are formed.

2. Compound (III) is obtained also when acetic acid is replaced by hydrochloric acid.

3. Compound (III) on heating with sodium hydroxide or with sulfuric acid is converted to 1,1'-dinaphthyl; in the case of sodium hydroxide,(1-hydroxy-1,2,3,4-tetrahydro)-1,1'-dinaphthyl-3-sulfonic acid (IV) is formed as an intermediate compound.

4. On reducing the oxime of the bisulfite compound of 1-naphthol with zinc and acetic acid,1-amino-1,2,3,4-tetrahydronaphthalene-3-sulfonic acid (V) is obtained.

5. The course of the reduction of the bisulfite compound of 1-naphthol and its oxime corresponds to that of the reduction of 1-hydroxy-1,2,3,4-tetrahydronaphthalene and its oxime and confirms the structural formulas of the bisulfite compound and its oxime proposed previously.

## LITERATURE CITED

[1] S. Bogdanov, J. Gen. Chem. 28, 1324 (1958).*

[2] J. v. Braun, O. Braunsdorf and G. Kirschbaum, Ber. 55, 3648 (1922).

[3] S. Bogdanov and N. Karandasheva, J. Gen. Chem. 26, 3365 (1956).*

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* Original Russian pagination. See C. B. Translation.

# ON THE SYNTHESIS OF CHOLINE AND THIOCHOLINE ESTERS OF CARBOXYLIC ACIDS

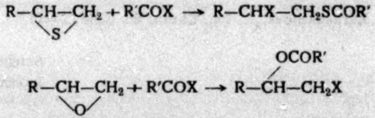
S. Z. Ivin

The methods described in the literature for the preparation of choline and thiocholine esters of carboxylic acids are, as a rule, multistage processes and cannot meet the renewed requirements for these esters. For example, acetylthiocholine iodide is prepared by the multistage method of Renshaw [1]. Choline esters of carboxylic acids are synthesized by the action of acyl chlorides on choline chloride [2]. The synthesis of choline esters by the addition of 2-chloroethyl esters of carboxylic acids to trimethylamine in benzene solution by heating to 100° is described in the literature. By this means esters of choline chloride and stearic, palmitic, lauric, caprylic acids, etc. have been prepared. However, the isolation of individual products was not achieved by this means [3].

As has already been reported, we have developed a new method of synthesizing thioacetylcholine iodide [4] which comprises two stages — the preparation of 2-iodoethyl acetate and its addition to trimethylamine.

This method was used also for the synthesis of other acylthiocholine halides and also of acylcholine halides.

The initial esters of 2-haloalkylthiolcarboxylic acids and of 2-haloalkylcarboxylic acids are readily obtained by the action of haloanhydrides on alkylene sulfides [4] and correspondingly on the alkylene oxides according to the scheme:



The reaction proceeds during a short interval of time with the formation of the corresponding esters in 70% yield.

Acylthiocholine halides and acylcholine halides are prepared by addition of the 2-haloalkylthiolcarboxylic and 2-haloalkylcarboxylic esters to trimethylamine in the cold in a medium of dry ether according to the scheme:

$$(CH_3)_3N + XCH(R)CH_2SCOR' \longrightarrow (CH_3)_3\underset{\overline{X}}{\overset{+}{N}}CH(R)CH_2SCOR'$$

$$(CH_3)_3N + XCH_2CH(R)OCOR' \longrightarrow (CH_3)_3\underset{\overline{X}}{\overset{+}{N}}CH_2CH(R)OCOR'$$

The 2-iodoalkylthiolacyl and 2-iodoalkylacyl compounds combine with trimethylamine considerably more easily and with better yields of the corresponding thiocholine and choline carboxylic acid esters than do the 2-bromoalkylthiolacyl and bromoalkylacyl compounds.

Acetylthiocholine iodide [4], acetylthiocholine bromide, butyrylthiocholine bromide, 1-methylacetylthiocholine iodide and the oxygen analogs – acetylcholine iodide, acetylcholine bromide, benzoylcholine bromide, acetyl-2-methylcholine iodide and acetyl-2-methylcholine bromide were prepared by the above-described method.

By the addition of methyl 2-bromopropionate to trimethylamine, 3-methoxypropionyltrimethylammonium bromide was obtained.

Thus the previously developed method for the preparation of acetylthiocholine iodide is of a general nature and is applicable to the synthesis of other thiocholine and choline esters of carboxylic acids.

## EXPERIMENTAL

Preparation of acetylthiocholine bromide. 9 g of 2-bromoethylthiol acetate and 20 ml of dry ether were placed in a round-bottomed flask. 3 g of trimethylamine was added gradually in small portions to the solution cooled to –15°. After each addition the flask was closed and shaken vigorously. At the end of the addition the flask was stoppered and left to stand in the cold for 4-5 hours and then for a further 2-3 days at room temperature.

The acetylthiocholine bromide formed as a precipitate was filtered off and crystallized twice from propyl alcohol. M. p. 213°. Yield 6 g (50%).

Found %: N 5.61; S 13.05; Br 33.1. $C_7H_{16}ONBrS$. Calculated %: N 5.79; S 13.2; Br 33.0.

The remaining thiocholine and choline esters of carboxylic acids were prepared similarly.

Preparation of butyrylthiocholine bromide. 15.5 g of 2-bromoethylthiol butyrate and 5 g of trimethylamine were taken for the reaction. The yield of butyrylthiocholine bromide was 9 g (45%). After recrystallizing twice from butyl alcohol the product melted at 140-143°.

Found %: S 12.0; Br 31.1; N 5.2. $C_9H_{20}ONBrS$. Calculated %: S 12.3; Br 30.7; N 5.4.

Preparation of acetyl-α-methyl-thiocholine iodide. For this preparation 14 g of 2-iodoisopropylthiol acetate and 3 g of trimethylamine were taken. 7.1 g (42%) of acetyl-α-methylthiocholine iodide was obtained. After recrystallizing twice from isopropyl alcohol the product melted at 231-235°.

Found %: S 10.2; I 35.5; N 4.3. $C_8H_{18}ONIS$. Calculated %: S 10.5; I 35.5; N 4.6.

Preparation of acetylcholine bromide. 10 g of 2-bromoethyl acetate and 3.5 g of trimethylamine were taken. The yield of acetylcholine bromide was 8.0 g (59%). After recrystallizing twice from ethanol the product melted at 143°.

Found %: Br 35.6; N 6.0. $C_7H_{16}O_2NBr$. Calculated %: Br 35.4; N 6.2.

Preparation of acetylcholine iodide. For this preparation 10.9 g of 2-iodoethyl acetate and 3 g of trimethylamine were taken. The yield was 9.1 g (65%). After recrystallizing twice from ethanol the product melted at 160-161°.

Found %: I 46.7; N 5.4. $C_7H_{16}O_2NI$. Calculated %: I 46.4; N 5.1.

Preparation of benzoylcholine bromide. 6 g of 2-bromoethyl benzoate and 1.7 g of trimethylamine were taken. The yield of benzoylcholine bromide was 4 g (52%). The product melted at 218°.

Found %: Br 31.21; N 5.35. $C_{12}H_{18}O_2NBr$. Calculated %: Br 31.0; N 5.42.

Preparation of acetyl-2-methylcholine bromide. For this preparation 16 g of 2-bromopropyl acetate and 5.5 g of trimethylamine were taken. The yield was 8.5 g (40%). M. p. 133-134°.

Found %: C 40.20; Br 33.50; N 5.65. $C_8H_{18}O_2NBr$. Calculated %: C 40.00; Br 33.35; N 5.83.

Preparation of acetyl-2-methylcholine iodide. 9.7 g of iodopropyl acetate and 2.5 g of trimethylamine were taken for the reaction. 8.0 g (66%) of acetyl-2-methylcholine iodide was obtained. M. p. 175°.

Found %: I 44.5; N 4.31. $C_8H_{18}O_2NI$. Calculated %: I 44.2; N 4.9.

Preparation of 3-methoxypropionyltrimethylammonium bromide. 15 g of methyl 2-bromopropionate and 5.3 g of trimethylamine were taken for the reaction. 13 g (65%) was obtained.

Found %: C 37.4; Br 35.45; N 6.0. $C_7H_{16}O_2NBr$. Calculated %: C 37.2; Br 35.4; N 6.2.

## SUMMARY

1. It is shown that the method developed previously for the preparation of acetylthiocholine iodide is of general application for the synthesis of choline and thiocholine esters of carboxylic acids.

2. Acetylthiocholine bromide, butyrylthiocholine bromide, acetyl-2-methylcholine bromide, acetylcholine bromide, acetylcholine iodide, acetyl-2-methylcholine iodide, acetyl-2-methylthiocholine iodide, benzoylcholine bromide and 3-methoxypropionyltrimethylammonium bromide have been prepared by this method.

## LITERATURE CITED

[1] R. R. Renshaw, P. F. Dreicbach et al, J. Am. Chem. Soc. 60, 1765 (1938).

[2] J. K. Cline, Ch. A. 28, 4075 (1934); U. S. Patent 1957443.

[3] F. Fourneau and J. Paye, Bull. Soc. Chim. 11, 544 (1914).

[4] S. Z. Ivin, J. Gen. Chem. 22, 267 (1952).*

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* Original Russian pagination. See C. B. Translation.

# REACTIONS OF AROMATIC NITRO COMPOUNDS

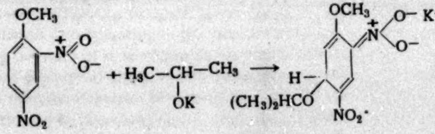
## III. A NEW METHOD FOR THE PREPARATION OF ALKYL ETHERS OF 2,4-DINITROPHENOL

S. S. Gitis and A. I. Glaz

Up to the present time the synthesis of alkyl ethers of 2,4-dinitrophenol has been carried out by one of the following three methods – the reaction of the silver salt of 2,4-dinitrophenol with alkyl halides on heating [1-3], from 2,4-dinitrochlorobenzene on heating with alcohols and alkali [4] or with alcoholates [5]. According to Wesson [3] ethers of the above alcohols prepared from 2,4-dinitrochlorobenzene always contain the latter as an impurity. We have shown recently [6] that the methoxyl group in 2,4,6-trinitroanisole can be replaced easily by other alkoxyl groups. As a result of this we have carried out a number of investigations with 2,4-dinitroanisole also, with the object of converting it to other ethers. It was shown that this conversion takes place readily at room temperature. We assume that in this case also the reaction proceeds by the mechanism suggested in the previous communication [6].

By this means we prepared in good yield from 2,4-dinitroanisole the ethyl, n-propyl, n-butyl, isobutyl and isoamyl ethers of 2,4-dinitrophenol.

It is interesting to note that the isopropyl ether of 2,4-dinitrophenol could not be prepared by this method because the colored intermediate product is not decomposed by water. Evidently the branched isopropyl group does take up a position alongside the methoxyl group but goes to the position ortho to the nitro group in the fourth position, thus excluding the possibility of replacement of the methoxyl group.



Our method has a number of advantages over those described in the literature. The 2,4-dinitrophenyl ethers are obtained in the pure state and, without recrystallization, have constants almost identical with those in the literature.

The 2,4-dinitrophenyl alkyl ethers can be isolated from solution in the corresponding alcohols and in benzene. Carrying out the reaction in benzene solution has the advantage that the uptake of the alcohol is reduced 5-10 times and that of alkali is halved. Moreover the yield of the ethers is increased on the average by 10%.

Since the methods of preparation of the ethers in solution in the alcohols and in benzene do not differ in principle we will give details of only one of the syntheses.

### EXPERIMENTAL

General method of preparing 2,4-dinitrophenyl ethers in benzene solution. 0.01 mole of 2,4-dinitroanisole was dissolved in 20 ml of benzene in the cold. To the solution was added 0.02 mole of potassium hydroxide dissolved by heating in 15-20 ml of the appropriate alcohol. The solution immediately acquired an orange-red color. After standing for an hour 50 ml of water was added to the solution and on shaking the color changed to yellow. The benzene solution was washed three times with water after which 30 ml of water was added to it and a ternary mixture (benzene-alcohol-water) was distilled off. The ether which remained behind collected under the water in the form of heavy, oily drops. After cooling, the liquid esters were separated from water and redistilled in vacuo, and the solid esters were recrystallized from ethanol. The experimental results are given in the table.

| Number | 2,4-Dinitrophenyl ether | Yield (in %) | Properties | |
|---|---|---|---|---|
| | | | our data | literature data [3] |
| 1 | Ethyl | 81 | M. p. 85-86° | 86° |
| 2 | n-Propyl | 83 | M. p. 29.5-30.5 | 30.5-31 |
| 3 | n-Butyl | 91 | B. p. 161.5-162 (0.1 mm) | 178-180 (2 mm) |
| 4 | Isobutyl | 85 | M. p. 30 | 30.3-31.5 |
| 5 | Isoamyl | 90 | B. p. 168-170 (0.2 mm) | 175-178 (1 mm) |

## SUMMARY

1. A new method is proposed for the preparation of higher alkyl ethers of 2,4-dinitrophenol.

2. The preparation of the 2,4-dinitrophenyl ethers confirms the mechanism previously put forward by us for the reaction between aromatic polynitro compounds and alcoholates.

## LITERATURE CITED

[1] Beilst. 6; Grüner, J. pr. Ch. I, 102, 227 (1867).

[2] H. Salkowsky and G. Kehs, Ber. 7, 137 (1874).

[3] J. Wesson, J. Am. Chem. Soc. 62, 3466 (1940).

[4] C. Wilgerodt, Ber. 12, 762 (1879).

[5] I. I. Blanksma and P. W. M. van der Wejden, Zbl. I, 864 (1942); Rec. trav. Chim. 59, 629 (1940).

[6] S. S. Gitis and A. I. Glaz, J. Gen. Chem. 27, 1897 (1957).*

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# ON THE LIQUID-PHASE CATALYTIC CHLORINATION OF METHYLCHLOROSILANES

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I. N. Uspenskaia and N. G. Ivanova

The preparation of chloro derivatives of methylchlorosilane, dimethyldichlorosilane and trimethylchlorosilane by means of gaseous chlorine under ultraviolet light irradiation or with sulfuryl chloride in the presence of benzoyl peroxide has been described in sufficient detail in the literature [1].

The photochemical chlorination of methylchlorosilanes results in the formation of a mixture of chloro derivatives of varying degrees of chlorination [2], and it has been established that the chloromethyl group chlorinates more readily than the unsubstituted methyl group [3, 4]. In recent papers [5, 6] much attention has been given to vapor-phase photochlorination of methylchlorosilanes, which enables monochloro derivatives to be separated from the reaction zone.

The chlorination of organosilicon compounds in the presence of azodiisobutyronitrile has not been described in the literature. For this reason it seemed of interest to examine the suitability of this method of chlorination for the preparation of chloromethylchlorosilanes.

It would be expected that such a chlorination of methylchlorosilanes would proceed according to the known stepwise mechanism and lead to the formation of all possible methyl-group substitution products.

It was in fact established that depending on the molar ratio of methylchlorosilane to chlorine the complete range of chloro derivatives of $CH_3SiCl_3$, $(CH_3)_2SiCl_2$ and $(CH_3)_3SiCl$ with chlorine atoms in the methyl groups can be prepared, the same mechanism operating in this case as in the photochlorination of methylchlorosilane. The main factor determining the ratio of monochloro derivatives to polychlorides is the degree of conversion of the initial silane to its chloro derivatives and the ratio, determined by this, of the initial methylchlorosilane to monochloro derivative in the reaction mixture. In view of the fact that chlorine in the silane methyl group accelerates the rate of substitution on further chlorination, liquid-phase chlorination of methylchlorosilanes aimed at the preparation of monochloro derivatives must therefore result in a considerable amount of unreacted methylchlorosilane remaining in the reaction mixture.

The extent to which the chlorine reacts and the content of monochloro derivative in the reaction mixture, which is connected with this, is determined to a large extent by the nature of the initial methylchlorosilane.

Thus whereas in the case of $(CH_3)_3SiCl$ practically complete absorption of the chlorine takes place and the reaction product is practically free from dichlorides and has 30% of monochloro derivative in the mixture, on chlorination of $CH_3SiCl_3$ only 10% of the chlorine is used up under these conditions and dichlorides are present in the reaction mixture which contains only 4% of the monochloro derivative. On chlorinating $(CH_3)_2SiCl_2$ under similar conditions the uptake of chlorine and the content of monochloride in the mixture of reaction products reach 60% and 24.5% respectively and in this case dichloro derivatives were not detected. An increase in the degree of chlorination of the methylchlorosilanes leads to the appearance of di- and polychloro derivatives in the reaction product, the quantity of which increases in passing from $(CH_3)_3SiCl$ to $CH_3SiCl_3$, for $(CH_3)_3SiCl$ and $(CH_3)_2SiCl_2$ they constitute 17.6 and 31.5% of the product respectively (with a content of combined chlorine in the chlorination products of 45-48%), and for $CH_3SiCl_3$ – 53.4% (with 16% chlorine).

| Expt. No. | Substance | Conditions of chlorination of methylchlorosilanes | | | Spec. grav. of react. mixt. after chlorination | Fract. comp. of react. mixt. after chlorination (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | temp. | molar ratio | | | un-changed silane | mono-chloro-deriv. | di- and poly-chloro deriv. | residue | loss |
| | | | silane/$Cl_2$ in react. mixture | silane/$Cl_2$ reacted | | | | | | |
| 1 | $CH_3SiCl_3$ | 50° | 1 : 0.37 | 1 : 0.035 | 1.2912 | 92.4 | 4.0 | — | 2.5 | 1.1 |
| 2 | | 60 | 1 : 0.53 | 1 : 0.16 | 1.3140 | 78.5 | 7.0 | 8.0 | 3.8 | 2.7 |
| 3 | | 60 | 1 : 0.70 | 1 : 0.32 | 1.3378 | 67.2 | 4.5 | 21.3 | 4.0 | 3.0 |
| 4 | $(CH_3)_2SiCl_2$ | 45—50 | 1 : 0.35 | 1 : 0.20 | 1.1326 | 67.4 | 24.5 | — | 4.5 | 3.6 |
| 5 | | 50 | 1 : 0.50 | 1 : 0.45 | 1.1993 | 48.2 | 29.2 | 13.4 | 5.5 | 3.7 |
| 6 | | 65—70 | 1 : 0.57 | 1 : 0.37 | 1.2173 | 55.1 | 20.1 | 13.3 | 6.2 | 5.3 |
| 7 | $(CH_3)_3SiCl$ | 45—50 | 1 : 0.38 | 1 : 0.32 | 0.9778 | 60.0 | 31.8 | 2.8 | 3.0 | 2.4 |
| 8 | | 45—50 | 1 : 0.50 | 1 : 0.48 | 0.9981 | 39.7 | 42.1 | 9.0 | 6.4 | 2.8 |
| 9 | | 45—50 | 1 : 0.82 | 1 : 0.80 | 1.0654 | 13.3 | 48.1 | 28.6 | 7.0 | 3.0 |
| 10 | | 45—50 | 1 : 0.91 | 1 : 0.90 | 1.1030 | 17.5 | 41.1 | 33.4 | 4.2 | 3.8 |

Note: The quantity of catalyst (on weight of silane) in experiments 1-7 was 0.3% and in experiments 8-10 – 0.2%.

In the catalytic chlorination of methylchlorosilanes as in the case of photochlorination of alkylchlorosilanes [7] an induction period (from 5 to 50 minutes) is observed at the beginning of the reaction.

Of the three methylchlorosilanes subjected to catalytic chlorination the most difficult to chlorinate is $CH_3SiCl_3$, this being shown by the longest induction period (up to 50 minutes), the highest rate of passage of chlorine throughout the entire chlorination process and the lowest degree of conversion of the initial silane to the chloro derivatives. The chlorination of $(CH_3)_3SiCl$ proceeds the most rapidly, the induction period being not longer than 5 minutes; the reactivity of $(CH_3)_2SiCl_2$ is intermediate between that of $CH_3SiCl_3$ and $(CH_3)_3SiCl$.

## EXPERIMENTAL

Chlorination of the methylchlorosilanes was carried out in glass columns (height 220 mm, diameter 25 mm) fitted with a long, spiral, reflux condenser, a distributor (a sintered glass plate) for the introduction of chlorine and a thermometer. A current of dry, gaseous chlorine was passed into the mixture of the methylchlorosilane and catalyst at the chosen temperature. The catalyst was added at the beginning of the reaction and a further few times according to the falling off of the rate of evolution of HCl. At the end of the chlorination, dry air was passed through to remove dissolved HCl. Separation of the mixture was effected by multiple fractional distillation at atmospheric pressure in a flask with a herring-bone fractionating column (length 400 mm). The composition of intermediate fractions was calculated from the density. The experimental results are given in the table.

## SUMMARY

1. The liquid-phase chlorination of the methylchlorosilanes – $CH_3SiCl_3$, $(CH_3)_2SiCl_2$ and $(CH_3)_3SiCl$ in the presence of azodiisobutyronitrile has been studied and it was established that by this method, depending on the molar ratio of silane to chlorine, the complete range of chloro derivatives containing chlorine atoms in the methyl group, can be obtained.

2. It was found that the same mechanism is operative in the liquid-phase catalytic chlorination of methylchlorosilanes as in photochlorination.

## LITERATURE CITED

[1] A. Ia. Iakubovich and V. A. Ginsburg, Progress in Chemistry 18, 46 (1949); K. A. Andrianov, Organosilicon Compounds [in Russian] (GONTI, 1955), pp. 121, 304.

[2] H. Gilman and R. O. Sauer, J. Am. Chem. Soc. 67, 1810 (1945).

[3] R. H. Krieble and J. R. Elliott, J. Am. Chem. Soc. 67, 1811 (1945); J. L. Speier, J. Am. Chem. Soc. 73, 825 (1951).

[4] Ch. Tamborcki and H. W. Post, J. Org. Ch. 1400 (1952).

[5] V. A. Ponomarenko and V. F. Mironov, Proc. Acad. Sci. USSR 94, 485 (1954).

[6] K. A. Andrianov, Ia. I. Mindlin and N. S. Leznov, Proc. Acad. Sci. USSR 94, 873 (1954).

[7] E. P. Mikheev, Proc. Acad. Sci. USSR 108, 484 (1956).*

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* Original Russian pagination. See C. B. Translation.

# IMPROVED METHODS OF SYNTHESIS OF PHENYLDICHLOROPHOSPHINE AND PHENYLPHOSPHINIC DICHLOROANHYDRIDE

E. L. Gefter

Phenyldichlorophosphine and phenylphosphinic dichloroanhydride are important intermediate products for the synthesis of various classes of aromatic organophosphorus compounds. However the methods of preparation of these chloroanhydrides (particularly of the first) have various deficiencies. Phenyldichlorophosphine can be prepared by several methods [1], two of which are of practical significance. 1) By the interaction of benzene and phosphorus trichloride in the gaseous phase [1]. This method requires cumbersome apparatus and a long continuous process; moreover there is always a substantial danger of fire and explosion. 2) By the interaction of benzene and phosphorus trichloride in the presence of aluminum chloride [1, 2]. This method is considerably simpler but on the negative side there is the necessity for complexing the catalyst before isolating the phenyldichlorophosphine (without this it is impossible to achieve good yields of the product) which is a troublesome and sometimes even a hazardous operation [2]. The maximum yield of phenyldichlorophosphine by the second method is 78% [2].

Phenylphosphinic dichloroanhydride can be synthesized by the oxidation of phenyldichlorophosphine with oxygen (a very dangerous method), with chlorine and phosphorus pentachloride, by the partial hydrolysis of phenyltetrachlorophosphine or by treating it with sulfur dioxide and finally by the interaction of phenylphosphinic acid with phosphorus pentachloride [1].

In the course of work on the development of more convenient and acceptable methods of synthesis of the two chloroanhydrides in question we have found that phenyldichlorophosphine can be prepared very simply, in complete safety and in better yields than those reported in the literature if after reacting benzene and phosphorus trichloride in the presence of aluminum chloride (in the molar ratios 1:3:1) the catalyst is combined with pyridine and the phenyldichlorophosphine is vacuum-distilled directly from the reaction flask. The yield of phenyldichlorophosphine is about 90% [3].

By treatment of phenyldichlorophosphine with chlorine, phenyltetrachlorophosphine was obtained and the latter (without isolation) gave phenylphosphinic dichloroanhydride in a yield of about 90% by reaction with sulfur dioxide. The general scheme of preparation of the two chloroanhydrides is indicated below.

$$C_6H_6 + 3PCl_3 + AlCl_3 \longrightarrow C_6H_5PCl_2 \cdot AlCl_3 + 2PCl_3 + HCl$$

$$C_6H_5PCl_2 \cdot AlCl_3 \xrightarrow{C_5H_5N} C_6H_5PCl_2 + AlCl_3 \cdot C_5H_5N \qquad (1)$$

$$C_6H_5PCl_2 + Cl_2 \longrightarrow C_6H_5PCl_4 \xrightarrow{SO_2} C_6H_5POCl_2 + SOCl_2 \qquad (2)$$

## EXPERIMENTAL

Phenyldichlorophosphine. In a four-necked, round-bottomed flask fitted with a dropping-funnel, a reflux condenser with a calcium chloride tube, a sealed stirrer and a thermometer, 39 g of benzene, 206 g of phosphorus trichloride and 70 g of aluminum chloride (molar ratios 1:3:1) were mixed. The mixture was refluxed for 3 hours with vigorous stirring. The hydrochloric acid which was copiously evolved was absorbed in water. The mixture was then cooled and the excess phosphorus trichloride was distilled off at 30-40 mm at a bath temperature of 50-55°. To the viscous, liquid residue 42 g of dry pyridine (molar ratio $AlCl_3 : C_5H_5N = 1:1$) was added with stirring, the reaction temperature being maintained at 40-50° by external cooling. The product obtained, which solidifies below 60-70°, was heated above its melting point and distilled in vacuo, with stirring, at 2-3 mm and a bath temperature of 90-155°, a low-boiling fraction being taken off first, followed by 83 g of crude phenyldichlorophosphine. After repeated redistillation 80 g (90%) of pure phenyldichlorophosphine was obtained, having b.p. 58-59° at 0.8-1 mm, $n^{20}D$ 1.5960, $d^{20}_4$ 1.3191, in conformity with the data in the literature [2]. On increasing the quantities of starting materials 12 times, the yield of phenyldichlorophosphine was 85-87%.

Phenylphosphinic dichloroanhydride. In a four-necked, round-bottomed flask fitted with a reflux condenser with a calcium chloride tube, a stirrer, a thermometer and a gas inlet tube was placed 1720 g of phenyldichlorophosphine dissolved in 1400 ml of carbon tetrachloride. The gas inlet tube was placed above the surface of the liquid and dry chlorine was passed through the system, with thorough stirring of the mixture. The reaction temperature was kept between the temperature limits of 10-20° by external cooling. The phenyltetrachlorophosphine precipitated in the form of yellowish-white crystals. After the exothermic reaction ceased (8 hours) chlorine was passed for a further 5-10 minutes; then the gas inlet tube was submerged in the semiliquid mass and dry, gaseous sulfur dioxide was passed into the system at 5-15° (again with stirring and external cooling) until the crystals completely disappeared and the reaction mixture was converted to a homogeneous yellow liquid. A low-boiling fraction was distilled off ($SO_2$, $SOCl_2$, $SO_2Cl_2$, $CCl_4$) and the residue was redistilled at 83-84° (1 mm). 1650 g (90%) of phenylphosphinic dichloroanhydride was obtained; $n^{20}D$ 1.5578, $d^{20}_4$ 1.1977, in conformity with the data in the literature [1].

## SUMMARY

Simple methods for the synthesis of phenyldichlorophosphine and phenylphosphinic dichloroanhydride in yields of about 90% of theory have been developed.

## LITERATURE CITED

[1] G. M. Kosolapoff, Organophosphorus Compounds, N. Y. (1950).

[2] B. Buchner and L. B. Lockhart, J. Am. Chem. Soc. 73, 755 (1951).

[3] E. L. Gefter, Author's Certificate 107266, Feb. 4, 1957.

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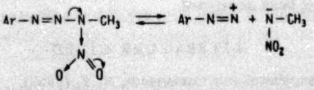
Scientific-Research Institute of Plastics

# THE STRUCTURE AND TRANSFORMATIONS OF METHYLARYL-N-NITROTRIAZENES

## III. ON SOME PROPERTIES OF METHYLARYL-N-NITROTRIAZENES

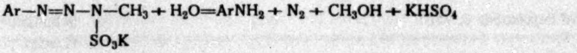
N. M. Baranchik, I. V. Grachev and D. Z. Zavel'skii

A study of the properties of methylaryl-N-nitrotriazenes has shown that the splitting of these compounds into their initial components takes place not only in acidic media as for methylaryl-N-triazenesulfonic acids [2, 3], but also in neutral media since the nitro group, being a more powerful electrophilic substituent than the sulfonic acid group polarizes the bond between the diazo and the amino components more strongly.



(I)

For the same reason it would be expected that the elimination of acyl groups in acidic media, characteristic of N-triazenesulfonic acids [3]



$$\underset{\textstyle SO_3K}{Ar{-}N{=}N{-}N{-}CH_3} + H_2O = ArNH_2 + N_2 + CH_3OH + KHSO_4 \qquad (II)$$

should occur more strongly in N-nitrotriazenes. However, investigations carried out in the present paper have shown that in media of pH from 1 to 7 at room temperature N-nitrotriazenes do not split off the slightest trace of nitric acid even over a period of 6 weeks. The same results are also shown on heating N-nitrotriazenes to boiling point in 68% sulfuric acid.

The unexpected strength of the bonds between nitro groups and the amino nitrogen of triazenes in acidic media, in comparison with the corresponding bonds in the case of sulfonic acid groups can, we suggest, be explained in the first place by the fact that the polarity of the bond between the two different elements, nitrogen and sulfur, is stronger than that between two nitrogens. In addition one should take into account Sidgwick's view [4] that in the bond between two nitrogens the two atoms evidently share a lone electron pair and this imparts additional strength to such bonds. The basis for this assumption is, according to Sidgwick, the fact that the heat of formation of an N═N bond is 2.54 times greater and of an N≡N bond 5.86 times greater than that of an ordinary N–N bond whereas the heat of formation of a C═C bond is only 1.79 times and of a C≡C bond 2.35 times greater than that of an ordinary C–C bond.

The tendency of a double bond between nitrogen atoms to be converted to a triple bond, with elimination of nitrogen is well known.

A similar tendency of a single bond between nitrogen atoms to be converted to a multiple bond can be observed in the action of acids on nitramines, and in particular, on methylnitramine. It was shown [5] that in this case nitrous oxide and methyl alcohol is formed.

$$CH_3{-}NH{-}NO_2 \longrightarrow N_2O + CH_3OH \qquad \text{(III)}$$

The action of acidic media on methylaryl-N-nitrotriazenes is exactly the same. Fission to the initial components first takes place according to reaction (I), which is favored by the strongly electrophilic nature of the nitro group, and the methylnitramine breaks down according to reaction (III).

We found an even greater difference between the properties of methylaryl-N-nitrotriazenes and methylaryl-N-triazenesulfonic acids in a study of the action of different alkalis and basic organic solvents on methylaryl-N-nitrotriazenes.

It has been reported previously [1] that N-nitrotriazenes cannot be recrystallized from such solvents as alcohol, benzene ether, etc. because they decompose during the process, with the evolution of gas. We have now found that N-nitrotriazenes dissolve readily in pyridine and somewhat less easily in triethylamine and certain other basic solvents. It was found that the solutions are colored, in the case of pyridine a deep red-brown and in triethylamine a bright orange.

Freshly prepared solutions of N-nitrotriazenes in basic solvents precipitate the unchanged initial materials on dilution with water. If however these solutions are allowed to stand for a few hours the N-nitrotriazenes do not separate on dilution, and on acidification of the dilute aqueous solutions diazo compounds and nitrous acid are found in considerable quantities.

It was shown that N-nitrotriazenes give orange-colored solutions in aqueous ammonia also. On keeping for 6 weeks at room temperature these solutions deposit crystals that prove to be the arylamines and diazo compounds that enter into the composition of the N-nitrotriazenes undergoing decomposition in the ammonia solution. In aqueous alkali solutions N-nitrotriazenes dissolve with a red or cherry color. If such solutions are kept for some time and are then extracted with ether, the extract, after removal of the ether, again contains arylamines. If the arylamine in question is volatile it can be isolated from the original solution in a fairly pure state, by steam distillation. Diazo compounds and nitrous acid are found on acidification of the solution remaining after extraction with ether or steam distillation.

The reactions described take place even more clearly in alcoholic potassium hydroxide solutions. N-nitramines dissolve readily in these with a deep cherry color. On diluting the solutions with a saturated, aqueous bicarbonate solution the N-nitrotriazene dissolved precipitates unchanged and after standing for 12 hours at room temperature, 32-34% of the arylamine and 31.5-32.5% of the sodium nitrite theoretically possible, as calculated from the initial triazene, can be isolated from the solutions.

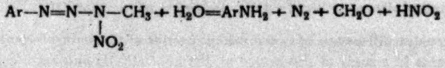
Most characteristic is the behavior of nitrotriazenes in sodium methylate solutions. For example, a solution of a triazene in methanol containing 1.2% $CH_3ONa$, on standing for 15 minutes after dissolving the triazene, precipitates 52% of the unchanged initial material on addition of water and bicarbonate. After 30 minutes only 35%, and after an hour only 13%, of the triazene can be recovered. Together with it correspondingly more amine and nitrite are found. Finally, 30.5% sodium methylate, within 1.5-2.0 hours after dissolving a nitrotriazene, brings about 76-78% conversion of the latter to the amine and 85% to nitrite.

Further investigation showed that in addition to the amine and nitrite, among the decomposition products formaldehyde can be detected; this was identified by its characteristic reactions with phenylhydrazine and sodium nitroprusside and also with phenylhydrazine and potassium ferricyanide. Quantitative analysis by means of hydroxylamine hydrochloride showed that the decomposition products of an N-nitrotriazene in a 16.5% sodium methylate solution, on standing for 1.5-2.0 hours contains 54-59% of the formaldehyde theoretically possible. At the same time under these conditions 43% of the arylamine and 53.5% of the nitrite was found.

It was observed that on allowing solutions of methylaryl-N-nitrotriazenes and sodium methylate to stand their dark-cherry color changes to brown but no gas is evolved. On adding aqueous bicarbonate to these solutions until there is no reaction for free sodium hydroxide (to thiazole paper) evolution of nitrogen is observed and this becomes more vigorous on heating.

Thus it was found that methylaryl-N-nitrotriazenes, containing no hydrogen attached to oxygen or nitrogen, which are normally pale-yellow in color dissolve in aqueous or alcoholic alkalis and in sodium methylate, giving bright-red or dark-brown solutions, and in pyridine, triethylamine and ammonia – dark-brown or orange solutions. On allowing the alkaline, and in particular the methylate, solutions to stand, their color changes and the methylaryl-N-nitrotriazenes dissolved undergo decomposition with the formation of arylamines, nitrite, formaldehyde and nitrogen. The arylamines formed in this way correspond in structure to the diazo compounds from which the triazene was synthesized.

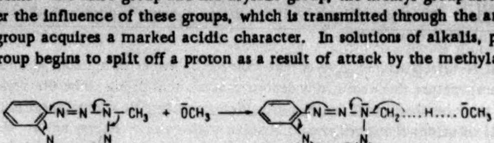
This decomposition reaction can be depicted by the following



$$Ar{-}N{=}N{-}\underset{NO_2}{\underset{|}{N}}{-}CH_3 + H_2O = ArNH_2 + N_2 + CH_2O + HNO_2 \qquad (IV)$$

In view of the inclusion of a molecule of water on the left side of the above equation this might have been considered to be a hydrolytic reaction. However, a more thoughtful examination shows that as a result of the reaction two component parts of the methylaryl-N-nitrotriazene, namely the diazo compound and the nitro group, are reduced to the amine and nitrous acid, and two other components, the methyl group and the two substituted nitrogens, are oxidized to formaldehyde and nitrogen.

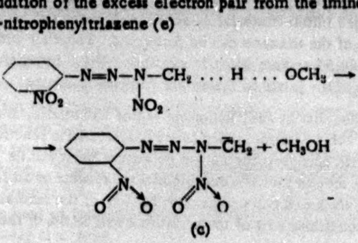
We consider that the reaction observed can be explained by the following considerations. In the methylaryl-N-triazenes the amino nitrogen to which the methyl group is attached is at the same time connected to two electrophilic substituents – the nitro group and the arylazo group; the methyl group also contains electrophilic substituents. Under the influence of these groups, which is transmitted through the amino nitrogen, the hydrogen of the methyl group acquires a marked acidic character. In solutions of alkalis, particularly of sodium methylate, the methyl group begins to split off a proton as a result of attack by the methylate anion.



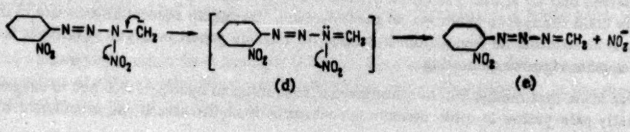
(V)

This results in a marked increase of the displacement of electrons toward the two electrophilic substituents because of the increased electron density on the carbon of the methyl group. A shift of part of the charge toward the nitro and arylazo groups naturally brings about a bathochromic effect, which is shown by the deep red color of methylate solutions of a methylaryl-N-nitrotriazene.

After the transition state (b) is broken down by complete removal of the proton (VI) the anion (c) is formed which cannot be stabilized in the form of the hypothetical compound (d) since the nitrogen next to the methylene group would have 10 electrons. Stabilization occurs by elimination of the nitro group (VII) which is converted to a nitrite anion by addition of the excess electron pair from the imino nitrogen, and the formation of the methylene derivative of o-nitrophenyltriazene (e)

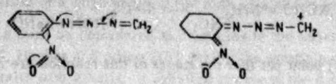


(VI)

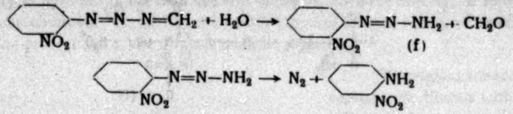


(VII)

Compound (e) would no longer be likely to be deeply colored because its bipolar structure would be too strained.

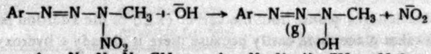


When the methylate solution, after standing, is diluted with water, acidified and heated, the azomethine (e) breaks down (VIII) into formaldehyde and the o-nitrophenyltriazene (f). The latter, being analogous to the extremely labile phenyltriazenes studied previously by Dimroth [6], breaks down to nitrogen and o-nitroaniline.



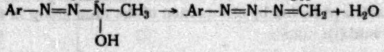
(VIII)

It was also suggested that the reaction under investigation proceeds possibly not through stages (V), (VI) and (VII) but through stages (X) and (XI).



$$Ar-N=N-\underset{NO_2}{\underset{|}{N}}-CH_3 + \bar{O}H \longrightarrow Ar-N=N-\underset{OH}{\underset{|}{N}}-CH_3 + N\bar{O}_2 \quad (g)$$

(X)

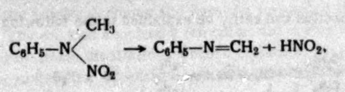


$$Ar-N=N-\underset{OH}{\underset{|}{N}}-CH_3 \longrightarrow Ar-N=N-N=CH_2 + H_2O$$

(XI)

In this case after replacement of the nitro group, which splits off as a nitrite ion, the arylazo-substituted methylhydroxylamine (g) must be formed. Such compounds were synthesized by Bamberger and his co-workers by the condensation of diazo compounds with methylhydroxylamine [7]. These N-hydroxytriazenes give in alcoholic solution a characteristic greenish-blue coloration with ferric chloride but split off water by the action of alkalis, with formation of azomethines. However, among the decomposition products of various methylaryl-N-nitrotriazenes in alcoholic alkali we never succeeded in detecting even traces of N-hydroxytriazenes. Hence this reaction proceeds through stages (V), (VI) and (VII).

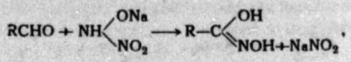
It should be borne in mind that Bamberger [8], while studying the properties of arylnitramines, which he called diazobenzenic acids, found that on refluxing phenylmethylnitramine, or its p-nitro derivative, with aqueous-alcoholic alkali for 40 hours, the arylamine, nitrite and formic acid were formed in considerable quantity. The author represented this reaction in the following way:



$$C_6H_5-N\begin{matrix} CH_3 \\ NO_2 \end{matrix} \longrightarrow C_6H_5-N=CH_2 + HNO_2,$$

and suggested that the formic acid found is a product of the Canizzaro reaction between formaldehyde and alkali, although he did not confirm the presence of methyl alcohol. Franchimont and van Erp [9] observed a similar reaction for aliphatic methylnitramines. However, the elimination of the nitro group in the cases of the authors mentioned took place with much more difficulty than in the case described by us.

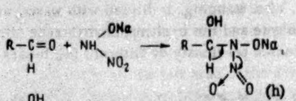
In many textbooks of organic and analytical chemistry [10] the Angeli reaction [11] is given as a method of determination of aldehydes. It involves the fact that by the action of aldehydes on the sodium salt of nitrohydroxylamine in aqueous solution, hydroxamic acid is formed, which gives a characteristic, intense red color with ferric chloride. This reaction can be represented by the following equation:



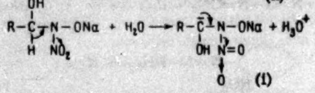
$$RCHO + NH\begin{matrix}ONa\\NO_2\end{matrix} \longrightarrow R-C\begin{matrix}OH\\NOH\end{matrix} + NaNO_2,$$

though Shlenk and Bergman [10] point out that the stages of this reaction are not clear.

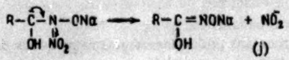
We consider that the Angeli reaction can be depicted by the following stages



(XII)



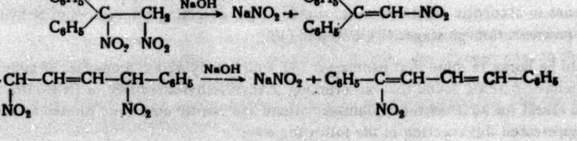
(XIII)



(XIV)

In this case the elimination of a proton from the carbon (XIII) of the addition product (XII) of the aldehyde and nitrohydroxylamine (h) takes place more easily because there is already a hydroxyl group in it. The carbanion (i) that is formed is stabilized further by elimination of the nitro group in the form of a nitrite ion, and the formation of hydroxamic acid (j).

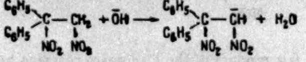
Our proposed reaction mechanism seems to us to explain satisfactorily all reactions whereby aliphatic C-nitro compounds split off the nitro group in the form of a nitrite ion in alkaline media, and undergo intramolecular re-arrangement of the bonds. For example, Wieland [12] found that $\alpha,\alpha$-diphenyl-$\alpha,\beta$-dinitroethane and 1,4-diphenyl-1,4-dinitrobutene split off nitrous acid in alkaline media with the formation of the corresponding $\alpha,\alpha$-diphenyl-$\beta$-nitroethylene and 1,4-diphenyl-1-nitrobutadiene-1,3



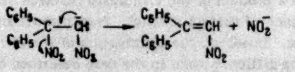
$$(C_6H_5)_2C(NO_2)-CH_2(NO_2) \xrightarrow{NaOH} NaNO_2 + (C_6H_5)_2C=CH-NO_2$$

$$C_6H_5-CH(NO_2)-CH=CH-CH(NO_2)-C_6H_5 \xrightarrow{NaOH} NaNO_2 + C_6H_5-C(NO_2)=CH-CH=CH-C_6H_5$$

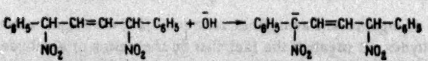
This seemingly strange reaction can easily be explained in the following way:



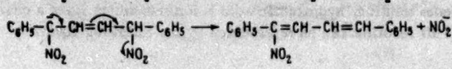
(XV)



(XVI)



(XVII)



(XVIII)

In the first place a proton splits off from the pseudo-acid under the action of the alkaline medium and the carbanion formed becomes stabilized by the formation of a double bond with the neighboring atom, suitable regrouping of other bonds and elimination of a nitro group in the form of a nitrite ion.

The reactions examined above must be considered as belonging to the series of nucleophilic elimination reactions studied in detail by Ingold, Hughes and others [13], taking the example of the interaction of alkyl halides and quaternary ammonium salts with alkalis. A detailed review of the mechanism of these reactions has been made by Reutov [14].

## EXPERIMENTAL

Behavior of 1-methyl-1-nitro-3-aryltriazenes in basic solutions. 1-Methyl-1-nitro-3-(2'-nitrophenyl)-triazene dissolves readily in pyridine in the cold and still better on moderate heating. A solution of an intense red-brown color is thereby obtained. On cooling the freshly prepared solution in ice, or on diluting with water, a light-yellow crystalline precipitate of the original triazene separates.

TABLE 1

Decomposition of an N-nitrotriazene in 1.2% $CH_3ONa$ Solution

| Time of standing of solution (in minutes) | Unchanged triazene isolated (in % of original) | Diazo compound found in triazene decomposition products (in %) |
|---|---|---|
| 15 | 52 | 30 |
|  | 52 | 29 |
| 30 | 35 | 43 |
|  | 30 | 37 |
| 60 | 13 | 43 |

The original triazene already fails to separate, on dilution with water, from a solution of the N-nitrotriazene in pyridine which has been kept for a few hours. On diluting with water and acidifying a pyridine solution of the triazene kept for 3-4 hours, nitrous acid (positive reaction with starch-iodine paper) and 2-nitrodiazobenzene (coupling with β-naphthol and determination of the azo dye formed) are detected in it. On similar treatment of a pyridine solution of the triazene kept for 24 hours, nitrous acid and the diazo compound are no longer detectable.

The N-nitrotriazene dissolves in triethylamine with more difficulty than in pyridine. Heating accelerates solution. The color of the solution is bright orange. On cooling the freshly prepared solution, crystals of the original triazene separate. The diazo compound can be detected on diluting with water and acidifying the triethylamine solution, after keeping the latter for a time.

Other methylaryl-N-nitrotriazenes behave similarly, including that obtained from 2,5-dichlorodiazobenzene, i.e., one not containing a nitro group on the aryl nucleus.

Behavior of 1-methyl-1-nitro-3-aryltriazenes in aqueous alkaline solutions. 0.5 g of 1-methyl-1-nitro-3-(2'-nitrophenyl)-triazene was added to 100 ml of 10% sodium hydroxide solution. In the cold the powder was not wetted. On heating to boiling the powder darkened and formed a suspension and finally rose to the surface in the form of a dark, fused resin. The solution acquired a red coloration during this treatment. After 5 days the reaction products were removed by steam distillation. Orange crystals of m. p. 69-70° (from alcohol) were isolated from the distillate by ether extraction. A mixture with authentic 2-nitroaniline (m. p. 72°) showed no melting point depression.

The suspension left after steam distillation was filtered and the filtrate was divided into two equal portions. o-Nitroaniline was isolated from the first half of the filtrate by ether extraction, since by treatment with nitrite in an acid medium it gave a diazo compound which formed azo dyes with R-salt and β-naphthol identical with those obtained from authentic o-nitrodiazobenzene.

The second half of the filtrate was acidified with hydrochloric acid, whereupon the solution became colorless. The acidified solution contained the diazo compound (coupling with β-naphthol) and nitrous acid (qualitative test with starch-iodine paper and with metanil-yellow).

1-Methyl-1-nitro-3-(2'-nitrophenyl)-triazene behaves similarly with sodium and potassium hydroxide solutions at other concentrations.

**TABLE 2**

Formation of o-Nitroaniline on Decomposition of 1-Methyl-1-nitro-3-(2'-nitrophenyl)-triazene in Sodium Methylate Solutions of Various Concentrations

| Content of CH$_3$ONa in solution (in %) | Quantity of amine found (in %) |
|---|---|
| 2.4 | 6.2<br>6.7 |
| 9.5 | 7.1 |
| 16.5 | 43.2<br>38.9 |
| 21.0 | 58.0<br>58.8 |
| 26.0 | 76.2<br>74.7<br>76.5 |
| 30.5 | 78.1<br>76.4 |

**TABLE 3**

Formation of Nitrite on Decomposition of 1-Methyl-1-nitro-3-(2'-nitrophenyl)-triazene in Sodium Methylate Solutions of Various Concentrations

| Content of CH$_3$ONa in solution (in %) | Quantity of nitrite found (in %) |
|---|---|
| 9.5 | 26.4 |
| 16.5 | 53.5 |
| 21.0 | 66.1 |
| 26.0 | 84.5 |
| 30.5 | 85.6 |

1-Methyl-1-nitro-3-(4'-nitrophenyl)-triazene dissolves in aqueous alkali solutions to give a cherry color. Ether extraction or steam distillation of alkaline solutions of the N-nitrotriazene after long standing yield p-nitroaniline, the diazo compound of which is a component for the synthesis of the original methyl-aryl-N-nitrotriazene.

If alkaline solutions of the N-nitrotriazene are acidified the diazo compound can be detected in them. If again the alkaline solutions are acidified after previous removal of p-nitroaniline by ether extraction or steam distillation, nitrous acid is found in addition to the diazo compound.

0.001 mole of 1-methyl-1-nitro-3-(4'-chloro-2'-nitrophenyl)-triazene was dissolved in 100 ml of 25% ammonia. The orange solution formed was kept at room temperature for 6 weeks. Crystals of m. p. 94° were formed at the bottom of the flask. After recrystallizing from alcohol they had m. p. 114-115° (4-chloro-2-nitroaniline melts at 116-117°). On treatment with nitrite in an acid medium the crystals formed 4-chloro-2-nitrodiazobenzene which was identified through the azo dyes formed by coupling with β-naphthol and R-salt.

Decomposition of methylaryl-N-nitrotriazenes in alcoholic alkali. 0.23 g of o-nitrophenylmethyl-N-nitrotriazene was dissolved in a 12% solution of potassium hydroxide in ethyl alcohol. To the transparent, dark-cherry colored solution a dilute aqueous bicarbonate solution was added gradually, with cooling; the color then changed to yellow, a turbidity appeared and nitrogen was evolved. The alcohol was distilled off in vacuo. The residual aqueous solution was extracted with ether until a fresh portion of ether did not become colored and a test portion of the aqueous solution continued to give a positive diazo reaction on acidification. The residue from the extract after removal of the ether was dissolved in hydrochloric acid and back-titrated with nitrite.

For determination of the nitrite content of the bicarbonate solution the latter after extraction with ether was added dropwise to an accurately weighed quantity of sulfamic acid, dissolved in 50 ml of 10% sulfuric acid, and the excess sulfamic acid was back-titrated with 0.1 N nitrite solution.

In two similar experiments 33.8 and 31.6% of the amine and 32.4 and 31.5% of the nitrite theoretically possible, was found. If the N-nitrotriazene is dissolved in alcoholic potassium hydroxide, diluted with water immediately and neutralized with bicarbonate, the nitrotriazene is recovered practically unchanged. (4-Chloro-2-nitrophenyl)-methyl-N-nitrotriazene also decomposes in alcoholic potassium hydroxide with the formation of the amine and nitrite.

Decomposition of methylaryl-N-nitrotriazenes in sodium methylate. To 0.001 mole N-nitrotriazene, accurately weighed, 20 ml of sodium methylate solution was added. Complete solution was effected in 5-10 minutes on shaking the stoppered flask. Sodium methylate in the following concentrations was used: 1.2, 2.4, 9.5, 16.5, 21.0, 26.0 and 30.5%. In the methylate solutions of strengths from 16.5 to 30.5% the triazene dissolved with a characteristic deep red cherry color. In the solutions of lower concentration an increasingly brown color was formed.

The above-mentioned coloration in sodium methylate is characteristic not only of methylaryl-N-nitrotriazenes containing a nitro group on the aryl nucleus but also of the N-nitrotriazene obtained from 2,5-dichlorodiazobenzene.

The behavior of solutions of methylaryl-N-nitrotriazenes in sodium methylate will be described below from the example of 1-methyl-1-nitro-3-(2'-nitrophenyl)-triazene.

Process of decomposition of a triazene in sodium methylate. A solution of the N-nitrotriazene in a 1.2% solution of sodium methylate was allowed to stand at room temperature for 15 minutes to 1 hour. The solution was then added dropwise, with good stirring, to 20 ml of 10% sulfuric acid cooled to 0-3° with ice. Light-yellow flakes separated out of the solution immediately. The suspension formed was filtered off rapidly on a sintered-glass filter, the solid product washed with ice-water, sucked off at the pump and dried in a vacuum desiccator to constant weight. The dried precipitate is a light-yellow powder showing the properties of N-nitrotriazenes: it has no clear melting point and ignites on moderate heating; with α-naphthylamine in glacial acetic acid it forms a brightly colored solution of the azo dye; in an alcoholic solution of β-naphthol crystals of the β-naphthol azo dye gradually precipitate.

The filtrate after separation of the unchanged triazene was analyzed for the quantity of diazo compound formed on pouring the methylate solution of the partially decomposed triazene into the acid. 20 ml of a 0.1 N alcoholic solution of β-naphthol, 30 ml of a concentrated acetate buffer solution and then bicarbonate to pH 6-7, were added to the filtrate with stirring. The excess β-naphthol, not used up in azo coupling, was back-titrated with a 0.1 N p-nitrophenyldiazonium salt solution. The analytical data are given in Table 1.

Determination of o-nitroaniline in the triazene decomposition products. a) A solution of the triazene in 21-26% sodium methylate after standing 1-2 hours was diluted with water and steam distilled. From the turbid, yellow distillate crystals of m. p. 70-71° (decomp.) were isolated. A mixed melting point with authentic o-nitroaniline showed no depression.

b) To a solution of the triazene in 21-26% sodium methylate, kept for 1.5-2.0 hours at room temperature, was added with cooling, first water and then saturated bicarbonate solution. The yellow solution which became turbid and evolved gas, was extracted with ether. Crystals of impure o-nitroaniline, which required several recrystallizations for purification, were isolated from the ether.

On treating the residue obtained from the ether extract with warm 20% hydrochloric acid the o-nitroaniline dissolves completely and a yellow-orange crystalline material is found in the solid residue. This substance when dissolved in α-naphthylamine, on heating (especially in the presence of a few drops of concentrated hydrochloric acid) gives the bright color characteristic of o-nitrophenylazo-β-naphthol in acetic acid. Hence it is the diazoamino compound, based on o-nitrodiazobenzene. The crude material (m. p. 177-180°) after recrystallizing from benzene and alcohol melted at 192°. It gave no melting point depression when mixed with 2,2'-dinitrodiazoaminobenzene (m. p. 195-196°). Hence, on neutralizing a solution of the triazene in sodium methylate, with bicarbonate, 2,2'-dinitrodiazoaminobenzene is formed in addition to o-nitroaniline.

c) To a solution of the triazene in sodium methylate, after standing for 1.5-2 hours at room temperature, 20 ml of a saturated solution of sodium bicarbonate was added. The reaction mixture changed color toward yellow, this effect being more marked at lower sodium methylate concentrations. The excess methyl alcohol was removed by heating on a water-bath at 30-35° for 30 minutes at reduced pressure.

After removal of the alcohol the solution was extracted with several portions of ether, the total volume of which was about 200 ml; the ether was distilled off on the water-bath and the residue treated with 50 ml of hot hydrochloric acid (d 1.12). The hydrochloric acid solution was diluted with water, cooled and titrated with 0.1 N sodium nitrite solution, the titer of which was determined by means of sulfamic acid.

The results of experiments on the determination of the quantities of o-nitroaniline formed on the decomposition of the triazene (sample weight 0.222-0.229 g) in sodium methylate solutions of various concentrations, are given in Table 2.

From the data of Table 2 it is seen that with increasing concentration of $CH_3ONa$ in the solution, the extent to which the N-nitrotriazene decomposes with the formation of o-nitroaniline also increases.

Determination of nitrous acid in the triazene decomposition products. To a solution of the triazene (about 0.224-0.227 g) in a sodium methylate solution that had been allowed to stand for 1.5-2 hours at room temperature, a saturated solution of sodium bicarbonate was added, the methanol was distilled off in vacuo over a period of 30 minutes and the o-nitroaniline formed was extracted with ether. The content of sodium nitrite in the aqueous alkaline solution, left after removal of o-nitroaniline, was determined. For this purpose the solution was evaporated on the water-bath until crystals of mineral salts began to separate, in order to remove residual ether and alcohol which interfere with the nitrite determination. Then to the solution was added a weighed quantity (about 0.0015 mole) of sulfamic acid and, with stirring, 70-100 ml of 10% sulfuric acid to a distinct acid reaction to Congo. The excess sulfamic acid was back-titrated with 0.1 N nitrite solution. The analytical data are shown in Table 3.

A solution of the triazene in 16.5% sodium methylate solution after standing at room temperature for 1.5-2 hours was treated with 20 ml of a saturated sodium bicarbonate solution and the methyl alcohol was distilled off in vacuo. The resulting solution was neutralized by mixing with 10% sulfuric acid to pH 8 and steam distilled. The distillate contained formaldehyde which was identified by the color reactions with phenylhydrazine and sodium nitroprusside [15] and with phenylhydrazine and potassium ferricyanide [16].

For the quantitative determination of formaldehyde in the triazene reaction products a sample of the triazene in sodium methylate was treated as described above and steam distilled. The distillate was collected below the surface of a solution of 15 ml of 0.1 N hydroxylamine hydrochloride in 35 ml of water until the total volume was 250 ml. The hydrochloric acid was back-titrated with 0.1 N sodium hydroxide potentiometrically, with a glass electrode, because coloration of the distillate by o-nitroaniline interfered with titration with an indicator. Control experiments showed that 96% of a known amount of formaldehyde can be found by the method described and that at pH 8 nitrous acid does not distill over from the solution which contains nitrite.

On titration of three samples of the triazene of 0.2250 g each, 5.5, 5.4 and 5.9 ml of 0.1 N alkali were required, corresponding to the formation of 54-59% of the formaldehyde theoretically possible for complete decomposition of the triazene.

Interaction of o-nitrophenyl-N-nitramine with sodium methylate solution. 0.001 mole of o-nitrophenyl-N-nitramine was dissolved in 20 ml of a 30% solution of sodium methylate in methanol. After 2 hours the solution was diluted with bicarbonate and extracted with ether. No trace of amine could be isolated from the ether. In another experiment the solution, after treatment with bicarbonate, was acidified to a positive reaction for mineral acid. No nitrous acid was found in the solution; only a trace of nitric acid was detected (by means of diphenylamine).

Behavior of N-nitrotriazenes in an acidic medium. a) Weighed quantities of the triazene were mixed with buffer solutions of pH from 1 to 7 and allowed to stand for 6 weeks. Each sample was then tested for nitric acid and amine.

For determination of nitric acid, sulfuric acid (about 60%) was added to a test portion, the solution was steam distilled and we tested for nitric and nitrous acids in the distillate. For determination of amine, the residue after distillation was neutralized with 10% alkali and extracted with ether. The ether was distilled from the extract and the residue was dissolved in concentrated hydrochloric acid and treated with nitrite. In none of the samples examined were even traces of either nitric acid or amine found.

b) A weighed sample of the triazene was heated in 68% sulfuric acid and the distillate was collected in water containing diphenylamine sulfate as an indicator for nitric acid. Nitric acid was not found in any of the test samples. The sulfuric acid solution from which the distillate was obtained was diluted with water and neutralized with strong alkali. The resulting solution was extracted with ether. The residue after removal of the ether from the extract, which was deep-yellow in color, was treated with acid and then with nitrite and added to a sodium carbonate solution of R-salt or β-naphthol. A coloration was obtained, indicating the presence of a small quantity of amine.

## SUMMARY

1. It has been established that in contrast to methylaryltriazene-N-sulfonic acids that split off the sulfonic

group in acidic media, N-nitrosubstituted methylaryltriazenes under the same conditions do not split off the nitro group but decompose to a phenol, nitrogen, an alcohol and nitrous oxide. Such reaction courses are explained by the high polarity of the bond between nitrogen and sulfur in comparison with that between two nitrogens.

2. It is shown that methylaryl-N-nitrotriazenes have the properties of pseudo acids. They dissolve in alkalis and in basic solvents with a marked deepening in color. On allowing these methylaryl-N-nitrotriazene solutions to stand they decompose with the formation of the arylamine, nitrite, nitrogen and formaldehyde.

3. An explanation of the mechanism of the decomposition reaction of methylaryl-N-nitrotriazenes in alkaline media is put forward, according to which a proton begins to split off from the methyl group under the action of hydroxyl or methoxyl, with the formation of an unstable carbanion which is then converted to the N-methylene derivative of the aryltriazene by fission of the nitro group in the form of a nitrite anion.

4. It is shown that the proposed mechanism explains satisfactorily the reactions of various aliphatic N-nitro and C-nitro derivatives taking place in alkaline media, with elimination of the nitro group in the form of a nitrite anion and with intramolecular rearrangement of bonds, and that such reactions must be included in the known class of nucleophilic elimination reactions.

## LITERATURE CITED

[1] N. M. Baranchik, L. V. Grachev and D. Z. Zavel'skii, J. Gen. Chem. 27, 117 (1957).*

[2] D. Z. Zavel'skii and L. A. Lishnevskaia, J. Gen. Chem. Coll. 1, 435 (1953).

[3] D. Z. Zavel'skii and L. A. Lishnevskaia, J. Gen. Chem. 25, 365 (1955).*

[4] N. V. Sidgwick, The Chemical Elements and Their Compounds, Oxford 1, 656 (1952).

[5] A. P. Franchimont, Rec. trav. chim. 17, 288 (1898); H. van Erp, Rec. trav. chim. 14, 1 (1895).

[6] O. Dimroth, Ber. 40, 2378 (1907); O. Dimroth and K. Pfister, Ber. 43, 2760 (1910).

[7] E. Bamberger and E. Renault, Ber. 30, 2283 (1897).

[8] E. Bamberger, Ber. 27, 371 (1894); 30, 1248 (1897).

[9] A. P. Franchimont and H. van Erp, Rec. trav. chim. 14, 235 (1895); 15, 165 (1896).

[10] A. E. Chichibabin, Basic Principles of Organic Chemistry (State Press, 103, 1931); V. Shlenk and E. Bergman, Organic Chemistry Vol. 1, (United Sci.-Tech. Press, 310 and 419, 1936); K. Bauer, Analysis of Organic Compounds (Russian translation), (Foreign Lit. Press, 176 (1953).

[11] A. Angeli and F. Angelico, Gazz. 30 (1), 593 (1900); 33 (2), 289 (1903).

[12] H. Wieland, Ber. 54, 1776 (1921); H. Wieland and F. Rahn, Ber. 54, 1770 (1921); H. Wieland and H. Stenzl, Ber. 40, 4825 (1907); Zbl. 1908, I, 361.

[13] E. Hughes, C. Ingold and A. Scott, J. Chem. Soc. 1937, 1271; E. Hughes, C. Ingold and V. Shapiro, J. Chem. Soc. 1937, 1277; K. Cooper, E. Hughes and C. Ingold, J. Chem. Soc. 1937, 1280.

[14] O. A. Reutov, Theoretical Problems in Organic Chemistry, Moscow State University Press, 114-137 (1956),**

[15] E. Rimini, Z. analyt. Ch. 42, 451 (1903).

[16] W. Friese and F. Richtsteiger, Pharm. Zentralhalle Deutschl. 81, 85 (1940).

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* Original Russian pagination. See C. B. Translation.

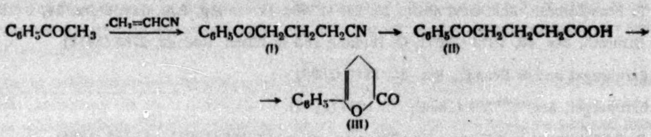
** In Russian.

## δ-LACTONES

### XII. SYNTHESIS AND PROPERTIES OF 6-PHENYL-3,4-DIHYDRO-α-PYRONE

M. Iu. Lur'e, I. S. Trubnikov, N. P. Shusherina and R. Ia. Levina

In our previous communications we described a method of synthesis of unsaturated δ-lactones (3,4-dihydro-α-pyrones) from monocyanoethylated aliphatic and alicyclic ketones [1-4]. In the present work the unsaturated δ-lactone, 6-phenyl-3,4-dihydro-α-pyrone (III), was prepared by this method from a monocyanoethylated aliphatic-aromatic ketone (acetophenone).

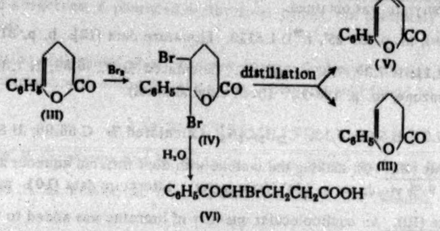


$$C_6H_5COCH_3 \xrightarrow{CH_2=CHCN} \underset{(I)}{C_6H_5COCH_2CH_2CH_2CN} \rightarrow \underset{(II)}{C_6H_5COCH_2CH_2CH_2COOH} \rightarrow$$

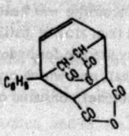
It is known from published data that cyanoethylation of acetophenone leads to the production of either the tricyanoethylated derivative [5], or of a mixture of monocyanoethylated (yield 13%) and dicyanoethylated acetophenone [6]. We have succeeded in finding conditions in which the cyanoethylation of acetophenone leads to the production of only the monocyanoethylated derivative, γ-benzoylbutyronitrile (I), in 28-35% yield. Hydrolysis of the nitrile (I) to γ-benzoylbutyric acid (II) and conversion of the latter to the lactone (III) took place with yields of 100 and 75% respectively.

Hydrolysis of the resulting unsaturated δ-lactone led to the formation of the original γ-benzoylbutyric acid, and alcoholysis and ammonolysis to the ester and amide respectively.

It was shown further that by the action of an equimolecular quantity of bromine on the lactone (III) a liquid dibromide (IV) is formed that fumes strongly in the air and, like the dibromolactones previously described by us [7, 8], is an extremely reactive compound. Thus the dibromolactone (IV) is converted on treatment with water to γ-bromo-γ-benzoylbutyric acid (VI) in 86.5% yield (as was shown by us previously [8] for other dibromolactones). On vacuum distillation in a current of dry air the dibromolactone is converted to 6-phenyl-α-pyrone (phenylcoumalin, V); however, simultaneously with phenylcoumalin (yield 14%) the original unsaturated δ-lactone (III) is formed. Thus, on distillation of the dibromolactone (IV), as well as elimination from it of two molecules of hydrogen bromide, which leads, as we have previously reported [7], to the formation of the α-pyrone (V), elimination of bromine with the formation of the original lactone also takes place.



The 6-phenylcoumalin (V) so obtained was characterized by the double maleic anhydride adduct (VII); by hydrolysis of the adduct and subsequent methylation the tetramethyl ester of the tetrabasic acid (VIII) was obtained.



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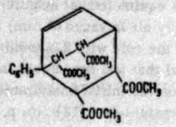

(VIII)

## EXPERIMENTAL

**γ-Benzoylbutyronitrile (I).** 48 g of acrylonitrile was added over a period of 3 hours, with vigorous stirring and water-cooling, to a mixture of 480 g of freshly redistilled* acetophenone and 2 ml of a saturated methanol solution of potassium hydroxide, at such a rate that the temperature did not exceed 25°. The reaction mixture was then stirred for a further 1-2 hours at room temperature and allowed to stand overnight; after the acetophenone was distilled off the residue was redistilled in vacuo. Monocyanoethylated acetophenone (I) was obtained in yields, in separate experiments, of 44 to 55 g, i.e., 28-35%.

B. p. 172-175° at 7-8 mm. Literature data: b. p. 178-182° at 8 mm, m. p. 38-39° (from alcohol) [6]; b. p. 125° at 1 mm, $n^{20}D$ 1.5326 [9].

Semicarbazone, m. p. 175° (from aqueous alcohol). Literature data [10]: m. p. 176-177° (from chloroform).

Found %: N 24.47, 24.26. $C_{12}H_{14}ON_4$. Calculated %: N 24.33.

**γ-Benzoylbutyric acid (II).** A mixture of 44 g of the nitrile and 240 ml of dilute (2:1) hydrochloric acid was refluxed for 3 hours. The crystals which separated on cooling (with shaking) were filtered off and dried (yield, quantitative). M. p. 125-126° (from water). Literature data: m. p. 126-127° [11].

**6-Phenyl-3,4-dihydro-α-pyrone (III).** A mixture of 25 g of γ-benzoylbutyric acid and 150 ml of acetic anhydride was refluxed for 5 hours, the acetic anhydride distilled off and the residue redistilled in vacuo. 6-Phenyl-3,4-dihydro-α-pyrone distilled at 174-175° (10 mm) and melted at 43-45° (from benzene or petroleum ether). Yield 17 g (75%). This compound is not described in the literature.

Found %: C 75.60, 75.42; H 5.88, 5.90. $C_{11}H_{10}O_2$. Calculated %: C 75.84; H 5.79.

The lactone obtained was easily hydrolyzed on heating with dilute alkalis, being converted to the original γ-benzoylbutyric acid (m. p. 125-126°).

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[*] Acetophenone that has been kept for a long time cyanoethylates with poorer yields or does not react at all.

Alcoholysis of the lactone (III). A solution of 12 g of the lactone in 60 ml of anhydrous alcohol was saturated with hydrogen chloride while cooling in ice water. After the usual treatment of the reaction mixture, 11.5 g (76%) of ethyl γ-benzoylbutyrate was obtained.

B. p. 178-180° (10 mm), m. p. 23-25°, $n^{20}$D 1.5110. Literature data [12]: b. p. 315°.

Found %: C 71.29, 71.11; H 7.30, 7.33. $C_{13}H_{16}O_3$. Calculated %: C 70.86; H 7.31.
2,4-Dinitrophenylhydrazone, m. p. 126-127° (from ethyl alcohol).

Found %: C 57.26, 57.27; H 5.29, 5.13. $C_{19}H_{20}O_6N_4$. Calculated %: C 56.98; H 5.04.

Ammonolysis of lactone (III). On shaking the lactone with concentrated aqueous ammonia, γ-benzoylbutyramide was obtained in 90% yield; m. p. 144° (from water). Literature data [10]: m. p. 144°.

Bromination of lactone (III). An equimolecular quantity of bromine was added to the lactone (III) in absolute ether, with cooling (in the absence of atmospheric moisture). The ether was evaporated in a current of dry air and the liquid dibromide (IV) which fumes in air, was redistilled in vacuo or reacted with water.

Vacuum distillation of the dibromolactone (IV). The liquid dibromide (IV), obtained from the bromination of 13 g of the lactone with an equimolecular quantity of bromine was heated for 0.5 hours (up to distillation temperature) in a current of dry air in vacuo (8 mm) and then slowly distilled. The distillate (6.5 g; b. p. 173-185° at 8 mm) was treated in the cold with 2 N sodium hydroxide for hydrolysis of the lactone (III)[*] to γ-benzoylbutyric acid. The material that was not soluble in alkali and which crystallized with difficulty on cooling (1.8 g: yield 14% calculated on the initial unsaturated lactone) consisted of 6-phenylcoumalin (V). M. p. 67.5° (from petroleum ether). Literature data [13]: m. p. 68°.

On acidification of the alkaline solution, γ-benzoylbutyric acid (4.7 g) was isolated. M. p. 125-126° (from water).

Isolation of 6-phenylcoumalin from the mixture containing the unsaturated δ-lactone (III) was also possible by prolonged boiling of the mixture with water because 6-phenylcoumalin is insoluble in water and does not react with it, and the unsaturated δ-lactone is hydrolyzed to γ-benzoylbutyric acid.

Maleic anhydride adduct of 6-phenylcoumalin. A mixture of 0.7 g (0.004 mole) of the pyrone (V) and 0.8 g (0.008 mole) of maleic anhydride in 4 ml of dry xylene was refluxed for 20 hours. 1.2 g (80%) of the double adduct (VII) was obtained. This compound is not described in the literature. M. p. 296-297° (from anhydrous acetone).

Found %: C 66.72, 66.82; H 3.88, 3.82. $C_{18}H_{12}O_6$. Calculated %: C 66.64; H 3.72.

On dissolving the adduct in 10% sodium hydroxide solution and subsequent acidification with hydrochloric acid a crystalline acid was obtained which titrated as tetrabasic; on treating a solution of this in ether with an ethereal solution of diazomethane the tetramethyl ester of (VII) was obtained. M. p. 191-192° (from aqueous alcohol).

Found %: C 63.19, 63.10; H 5.91, 6.09. $C_{22}H_{24}O_8$. Calculated %: C 63.48; H 5.80.

γ-Bromo-γ-benzoylbutyric acid. The dibromide (IV) obtained from 13 g of the lactone was treated with cold water, with mechanical stirring. The crystals of γ-bromo-γ-benzoylbutyric acid that separated were filtered off and dried. Yield 17.5 g (86.5%). M. p. 96-97° (from $CCl_4$). Literature data [14]: m. p. 97-98°. A mixed melting point with a sample of the same acid prepared by direct bromination of γ-benzoylbutyric acid was not depressed.

Found %: C 49.07, 49.09; H 4.18, 4.10. $C_{11}H_{11}O_3Br$. Calculated %: C 48.72; H 4.09.

## SUMMARY

1. A method has been developed for the preparation of monocyanoethylated acetophenone (γ-benzoylbutyronitrile) in yields of 28-35%.

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[*] The lactone (III) could be isolated by careful fractional distillation of the distillate (in a current of dry air). B. p. 174-176° (10 mm), m. p. 40-41° (from benzene).

2. By hydrolysis of γ-benzoylbutyronitrile to γ-benzoylbutyric acid and subsequent heating with acetic anhydride the unsaturated δ-lactone, 6-phenyl-3,4-dihydro-α-pyrone, not previously described in the literature, was obtained (in 75% yield).

3. From the dibromide of 6-phenyl-3,4-dihydro-α-pyrone, 6-phenylcoumalin was obtained (yield 14%) by distillation, and on treatment with water, it gave γ-benzoylbutyric acid (yield 86.5%).

## LITERATURE CITED

[1] R. Ia. Levina, N. P. Shusherina and M. Iu. Lur'e, J. Gen. Chem. 24, 1439 (1954).*

[2] N. P. Shusherina, R. Ia. Levina, M. Iu. Lur'e and V. I. Zdanovich, Reports, Moscow State University No. 10, 123 (1955).

[3] R. Ia. Levina, N. P. Shusherina, M. Iu. Lur'e and N. D. Orlova, Proc. Acad. Sci. USSR 106, 279 (1956).*

[4] N. P. Shusherina, R. Ia. Levina and M. Iu. Lur'e, J. Gen. Chem. 26, 750 (1956).*

[5] H. Bruson and T. Riener, J. Am. Chem. Soc. 64, 2850 (1942); A. P. Terent'ev and A. N. Kost, Reports, Moscow State University No. 12, 71 (1950).

[6] A. Campbell and J. Stevens, J. Chem. Soc. 959 (1956).

[7] N. P. Shusherina, M. Iu. Lur'e and R. Ia. Levina, Proc. Acad. Sci. USSR 109, 117 (1956).

[8] R. Ia. Levina, N. P. Shusherina, and M. Iu. Lur'e, Proc. Acad. Sci. USSR 113, 820 (1957).

[9] N. Albertson, J. Am. Chem. Soc. 72, 2597 (1950).

[10] C. Allen and W. Ball, J. Am. Chem. Soc. 59, 686 (1937).

[11] C. Voho and R. Levine, J. Am. Chem. Soc. 74, 5597 (1952).

[12] J. Wislicenus and C. Kuhn, Lieb. Ann. 302, 220 (1898).

[13] J. Kalff, Rec. trav. chim. 46, 594 (1927); G. Ciamician, Ber. 27, 841 (1894).

[14] R. Fuson, M. Davis, B. Wojcik and J. Turck, J. Am. Chem. Soc. 56, 235 (1934).

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# PREPARATION OF OXIDES OF α,β-UNSATURATED HIGHER FATTY ACIDS AND STUDY OF THEIR PROPERTIES

## P. A. Artamonov

The first researches on the preparation of the oxide of elaidic acid and study of its properties were carried out by A. A. Al'bitskii [1]. It was first observed by G. V. Pigulevskii that on oxidation of oleic, linoleic and linolenic acids with Prilezhaev's reagent, oxygenated derivatives were obtained, i.e., oxides [2-4]. Subsequently a number of investigators have been concerned with the preparation of oxides of unsaturated higher fatty acids [5-12].

It is known that the oxides of unsaturated higher fatty acids are highly reactive. The most characteristic reaction is their interaction with water with the formation of dihydroxy acids [3,6,9,13,14].

The oxides can also be hydrogenated. The addition of hydrogen to oxides is of great interest since it brings about the possibility of conversion of unsaturated fatty acids, from which the oxides are readily prepared, to hydroxy fatty acids. This enabled G. V. Pigulevskii and Z. Ia. Rubashko [15, 16], who were the first to investigate the catalytic hydrogenation of the oxides of oleic and erucic acids, to put forward a new method of preparation of hydroxy acids.

We were interested to prepare oxides of unsaturated fatty acids with the oxide ring in the position adjacent to the carboxyl group and to study their properties, since there is no information on such oxides in the literature. For the solution of this problem we oxidized the trans-isomers of the following fatty acids with benzoyl hydroperoxide (perbenzoic acid): hexadecen-2-acid-1 (2-hexadecanoic acid), octadecen-2-acid-1 (2-octadecanoic acid) and docosen-2-acid-1 (2-docosanoic acid).

Our investigations showed that the free acids react very slowly with benzoyl hydroperoxide (perbenzoic acid). In view of this we decided to oxidize the methyl esters of the acids. This enabled the oxidation process to be accelerated considerably and the oxides of the acids mentioned to be obtained in satisfactory yields (Table 2).

In order to study the chemical properties of the oxides obtained the latter were hydrated and hydrogenated.

It was found that the oxides prepared by us are readily hydrated on boiling with distilled water, acidified with a few drops of sulfuric acid. As a result of the hydration of the oxides investigated 2,3-dihydroxyhexadecanoic acid, 2,3-dihydroxyoctadecanoic and 2,3-dihydroxydocosanoic acids were obtained and characterized (Table 3).

On hydrogenation of the oxides investigated by us in ethyl alcohol in the presence of platinum black as catalyst, the monohydroxy acids were obtained, and on opening of the oxide ring the hydroxyl group evidently takes up the position furthest from the carboxyl group since the hydrogenation products that we obtained, according to their properties, corresponded to 3-hydroxyhexadecanoic, 3-hydroxyoctadecanoic and 3-hydroxydocosanoic acids (Table 4). Their melting points are considerably lower than the corresponding 2-hydroxy acids. Mixed melting points with the 2-hydroxy acids gave a depression but with 3-hydroxyhexadecanoic, 3-hydroxyoctadecanoic and 3-hydroxydocosanoic acids there was no depression.*

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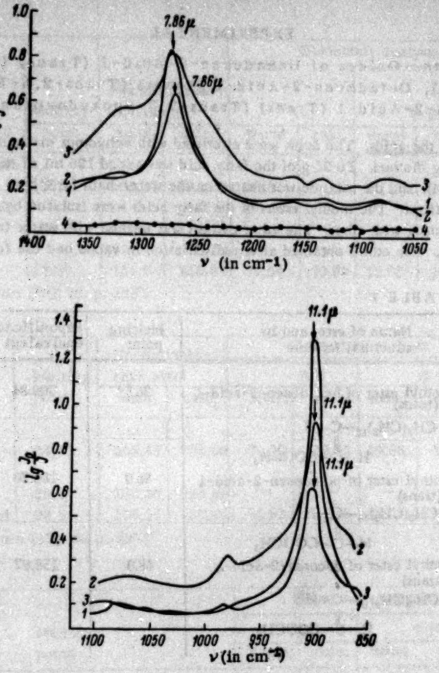
* 2-Hydroxyhexadecanoic, 2-hydroxyoctadecanoic and 2-hydroxydocosanoic acids, required for comparison, were prepared by the method of Ponzio [17] and Le Sueur [18], and 3-hydroxyhexadecanoic, 3-hydroxyoctadecanoic and 3-hydroxydocosanoic acids were prepared by the method of Eckert and Haller [19].



Infrared absorption spectra. 1) Hexadecen-2-acid-1 (trans) oxide (trans-2,3-epoxyhexadecanoic acid), 2) octadecen-2-acid-1 (trans) oxide (trans-2,3-epoxyoctadecanoic acid), 3) docosen-2-acid-1 (trans) oxide (trans-2,3-epoxydocosanoic acid).

In order to determine the position of the hydroxyl groups in the hydroxy acids obtained, the latter were oxidized with chromic acid in glacial acetic acid. From this oxidation keto acids were obtained with properties in close agreement with those of 3-ketohexadecanoic, 3-ketooctadecanoic and 3-ketodecosanoic acids (Table 5).

Hence, on hydrogenation of these oxides, opening of the oxide ring in fact takes place on the side nearest to the carboxyl group. This agrees with statements in the literature [10,15,16].

For complete characterization of the oxides investigated their absorption spectra in the infrared region were recorded (see Figures). It was found that in the spectra of the oxides in question there are intense, clearly defined, absorption bands with maxima at 11.1μ (about 900 $cm^{-1}$) and 7.86μ (about 1275 $cm^{-1}$), a little displaced toward the shorter-wave side of the spectrum resulting from the conjugation of the oxide ring with the C=O group of the carboxyl, since according to the literature [20, 21] these absorption maxima for the oxide of elaidic acid, where the oxide ring occurs between carbon atoms 9 and 10 (i.e., in the center of the molecule), are at 11.2μ (893 $cm^{-1}$) and 8.0μ (1250 $cm^{-1}$).

## EXPERIMENTAL

### 1. Preparation of the Oxides of Hexadecen-2-Acid-1 (Trans) (Trans-2,3-Epoxy Hexadecanoic Acid), Octadecen-2-Acid-1 (Trans) (Trans-2,3-Epoxyoctadecanoic Acid), and Docosen-2-Acid-1 (Trans) (Trans-2,3-Epoxydocosanoic Acid)

a) Esterification of the acids. The acids were esterified with anhydrous methanol in the presence of sulfuric acid by the following method. To 25 g of the fatty acid was added 125 ml of methyl alcohol containing 9 g of sulfuric acid (d 1.84), and the mixture was heated on the water-bath for 1 hour with continuous mechanical stirring with a glass stirrer. The methyl esters of the fatty acids were isolated by diluting the reaction mixture with water and extracting with ether. The ether extract was washed with water to neutral reaction, dried and the ether distilled off. The ethers obtained after redistillation in vacuo had the following properties (Table 1).

TABLE 1

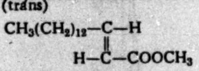
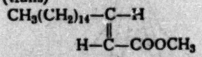
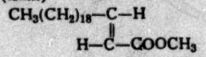
| Name of ester and its structural formula | Melting point | Saponification equivalent |
|---|---|---|
| Methyl ester of hexadecen-2-acid-1 (trans)  $CH_3(CH_2)_{12}{-}C{-}H \;=\; H{-}C{-}COOCH_3$ | 26.5° | 208.84 |
| Methyl ester of octadecen-2-acid-1 (trans)  $CH_3(CH_2)_{14}{-}C{-}H \;=\; H{-}C{-}COOCH_3$ | 36.0 | 188.20 |
| Methyl ester of docosen-2-acid-1 (trans)  $CH_3(CH_2)_{18}{-}C{-}H \;=\; H{-}C{-}COOCH_3$ | 48.0 | 158.82 |

TABLE 2

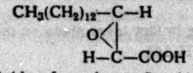
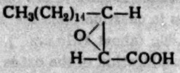
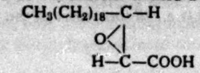
| Name of oxide and its structural formula | M.p. | Neutralization equivalent | | Elementary analysis | | | |
|---|---|---|---|---|---|---|---|
| | | | | % C | | % H | |
| | | found | calc. | found | calc. | found | calc. |
| Oxide of hexadecen-2-acid-1 (trans)  | 78.5° | 206.84 | 207.63 | 70.85 | 71.04 | 11.24 | 11.18 |
| Oxide of octadecen-2-acid-1 (trans)  | 83.5 | 187.87 | 188.10 | 72.35 | 72.41 | 11.60 | 11.48 |
| Oxide of docosen-2-acid-1 (trans)  | 89.5 | 158.91 | 158.35 | 74.50 | 74.50 | 12.01 | 11.94 |

TABLE 3

| Name of dihydroxy acid | Melting point | Neutralization equivalent |  | Elementary analysis |  |  |  | Number of OH-groups found (Zerewitinoff method) |
|---|---|---|---|---|---|---|---|---|
|  |  |  |  | % C |  | % H |  |  |
|  |  | found | calc. | found | calc. | found | calc. |  |
| 2,3-Dihydroxyhexadecanoic acid | 116.5° | 195.35 | 194.04 | 66.57 | 66.66 | 11.18 | 11.19 | 2.79 |
| 2,3-Dihydroxyoctadecanoic acid | 126.5° | 177.5 | 174.40 | – | – | – | – | 2.91 |
| 2,3-Dihydroxydocosanoic acid | 130.0 | 150.0 | 150.69 | 70.94 | 70.90 | 12.08 | 11.91 | 2.98 |

° According to the literature [18], m. p. 126°.

TABLE 4

| Hydroxy acid | Melting point | Neutralization equivalent |  | Elementary analysis |  |  |  | Number of OH groups found (Norman method) |
|---|---|---|---|---|---|---|---|---|
|  |  |  |  | % C |  | % H |  |  |
|  |  | found | calc. | found | calc. | found | calc. |  |
| 3-Hydroxyhexadecanoic acid | 84.5° | 205.68 | 206.09 | 70.29 | 70.52 | 12.06 | 11.84 | 0.96 |
| 3-Hydroxyoctadecanoic acid | 88.0° | 186.30 | 186.85 | – | – | – | – | 1.01 |
| 3-Hydroxydocosanoic acid | 92.5 | 158.17 | 157.44 | 73.93 | 74.08 | 12.39 | 12.45 | 1.0 |

° According to the literature [18], m. p. 89°.

TABLE 5

| Keto acid | Melting point | Elementary analysis |  |  |  |
|---|---|---|---|---|---|
|  |  | % C |  | % H |  |
|  |  | found | calc. | found | calc. |
| 3-Ketohexadecanoic | 94.0° | 70.86 | 71.04 | 11.10 | 11.18 |
| 3-Ketooctadecanoic | 98.2° | – | – | – | – |
| 3-Ketodocosanoic | 105.0 | 74.58 | 74.50 | 11.84 | 11.94 |

° According to the literature [22], m. p. 99°.

(b) Oxidation of the methyl esters with benzoyl hydroperoxide (perbenzoic acid). To 5 g of the methyl ester of the unsaturated acid an ethereal solution of benzoyl hydroperoxide (perbenzoic acid) (0.01158 g of active oxygen in 1 ml of solution) was added in an amount corresponding to 100% excess over the quantity of active oxygen theoretically required. The mixture was heated on the water-bath to 30-40° in 2 hours, after which it was allowed to stand overnight at room temperature. A large quantity of hot water was then added and the oxide of the fatty acid ester which formed an upper layer was extracted with ether after cooling. The ethereal solution was washed twice with water, dried and filtered and the ether was distilled off. The oxide of the methyl ester obtained was saponified with alcoholic alkali and the soap obtained, after removal of the alcohol, was treated with 20% sulfuric acid solution. The fatty acid oxide which separated was extracted with ether. The ethereal solution was washed with water to neutral reaction, dried and filtered. After removal of ether the oxide obtained was reduced to a fine powder in a porcelain dish, washed with a ten-fold quantity of petroleum ether to remove impurities, and filtered through an ordinary filter-paper. The analysis of the oxides made by this method is given in Table 2.

The yield of oxide varied between the limits 40-50%. In outward appearance they consist of white, fine-crystalline powder, readily soluble in ethyl ether, chloroform, acetone and alcohol. In petroleum ether they dissolve only on slight warming.

## 2. Study of the Chemical Properties of the Oxides

a) Hydration of the oxides. To 1.0 g of the oxide, 100 ml of distilled water acidified with 3-5 drops of conc. $H_2SO_4$ was added and the mixture was refluxed for 1-1.5 hours. On cooling the dihydroxy acid separated at the surface of the liquid in the form of white flakes. In order to separate it from the acid solution, the mixture was filtered through an ordinary filter-paper. The residue on the filter was washed to neutral reaction and dried, first between sheets of filter-paper and then in the air, and recrystallized twice from chloroform. The yield of dihydroxy acid varied between the limits of 85-95%. The results of examination of the dihydroxy acids obtained are given in Table 3.

b) Hydrogenation of the oxides. 10 ml of a 0.330 M alcoholic solution of the oxide was placed in each of two glass vessels ("ducks"), which were fixed on a shaker and connected to two burettes filled with electrolytic hydrogen. After the systems had been swept through with hydrogen the catalyst was introduced (0.09 g of platinum black) and shaking begun. The hydrogen absorbed at definite intervals was calculated. The volume of hydrogen absorbed was brought to 0° and 760 mm. On hydrogenation of the oxide of hexadecen-2-acid-1 (trans) (trans-2,3-epoxyhexadecanoic acid), 82.9 ml of hydrogen was absorbed, the oxide of octadecen-2-acid-1 (trans) (trans-2,3-epoxyoctadecanoic acid oxide) — 74.9 ml of hydrogen and the oxide of docosen-2-acid-1 (trans) (trans-2,3-epoxydocosanoic acid) — 62.9 ml (the calculated quantities of $H_2$ are 82.9, 75.0 and 63.2 ml respectively). The hydrogenation products of the oxides are fine-crystalline, white powders with high melting points and are evidently 3-monohydroxy acids. The results of analysis of the hydroxy acids obtained are given in Table 4.

Proof of the position of the hydroxyl groups in the 3-monohydroxy acids obtained. To 3 g of the hydroxy acid dissolved in 30 ml of glacial acetic acid 35 ml of an acetic acid solution, containing the theoretically required quantity of chromic anhydride, was added gradually with shaking over a period of 30 minutes. The reaction mixture was allowed to stand overnight. It was then heated on the water-bath for 10 minutes. On cooling and diluting with water a fine-crystalline precipitate separated which was filtered off and washed with water. After two recrystallizations from ethyl alcohol the keto acids obtained had constant melting points (Table 5).

## SUMMARY

1. The oxides of hexadecen-2-acid-1 (trans) (trans-2,3-epoxyhexadecanoic acid), octadecen-2-acid-1 (trans) (trans-2,3-epoxyoctadecanoic acid) and docosen-2-acid-1 (trans) (trans-2,3-epoxydocosanoic acid) have been synthesized for the first time and the properties of these oxides have been studied.

2. It was found that the oxides obtained are easily hydrated to form dihydroxy acids. 2,3-Dihydroxyhexadecanoic, 2,3-dihydroxyoctadecanoic and 2,3-dihydroxydocosanoic acids were obtained, of which the first and third are not described in the literature.

3. On hydrogenation the oxides form hydroxy acids. The opening of the oxide ring is such as to place the hydroxyl group on the carbon atom furthest away from the carboxyl group. 3-Hydroxyhexadecanoic, 3-hydroxyoctadecanoic and 3-hydroxydocosanoic acids were obtained, of which the first and last are not described in the literature.

4. The infrared absorption spectra of the oxides of hexadecen-2-acid-1 (trans) (trans-2,3-epoxyhexadecanoic acid), octadecen-2-acid-1 (trans) (trans-2,3-epoxyoctadecanoic acid) and docosan-2-acid-1 (trans) (trans-2,3-epoxydocosanoic acid) have been recorded.

# LITERATURE CITED

[1] A. A. Al'bitskii, J. Russ. Chem. Soc. 31, 76 (1899).

[2] G. V. Pigulevskii, J. Russ. Chem. Soc. 48, 1763 (1916).

[3] G. V. Pigulevskii and M. A. Petrova, J. Russ. Chem. Soc. 58, 1062 (1926).

[4] G. V. Pigulevskii and A. Ia. Vasil'ev, J. Russ. Chem. Soc. 61, 988 (1929).

[5] A. Steger and L. van Loon, Rec. trav. chim. 46, 703 (1927).

[6] J. Bőeseken and R. Belinfant, Rec. trav. chim. 45, 914 (1926); J. Bőeseken, R. Belinfant and W. Smit, Rec. trav. chim. 32, 377 (1929); W. Smit, Rec. trav. chim. 49, 539, 681 (1930).

[7] C. Doree and A. Pepper, J. Chem. Soc. 477 (1942).

[8] D. Warmbrun and A. Stutzer, Ber. 36, 3604 (1903).

[9] K. Bauer and O. Bähr, J. pr. Ch. 122, 201 (1929).

[10] C. Mack and W. Bickford, J. Org. Ch. 18, 686 (1953).

[11] Kora-Hashi, J. Soc. Chem. Ind. Japan 39, 162 (1936).

[12] D. Swern, J. Am. Chem. Soc. 66, 1925 (1944); 69, 692 (1947); 70, 1235 (1948); Chem. Rev. 45, 1 (1949); Org. Reactions, 7, 378 (1953).

[13] G. V. Pigulevskii and N. A. Simonova, J. Gen. Chem. 9, 1928 (1939).

[14] Heterocyclic Compounds, Ed. R. El'derfil'd (Elderfield) I, 5 [Russian translation] (Moscow, 1953).

[15] G. V. Pigulevskii and Z. Ia. Rubashko, J. Gen. Chem. 8, 829 (1938).

[16] G. V. Pigulevskii and Z. Ia. Rubashko, J. Gen. Chem. 25, 2227 (1956).*

[17] S. Ponzio, Gazz. 34, 77 (1904).

[18] H. Le Sueur, J. Chem. Soc. 85, 1708 (1904).

[19] A. Eckert and O. Haller, Monatsh. 34, 1815 (1913).

[20] O. Shreve, M. Heether, H. Knight and D. Swern, Anal. Chem. 23, 277 (1951).

[21] O. O'Konor and M. Heether, J. Org. Ch. 18, 603 (1953).

[22] R. Holman and W. Lundberg, Progress in the Chemistry of the Lipids, London-N.Y. 3, 233 (1955).

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# SUBSTANCES CAPABLE OF COMPLEX FORMATION

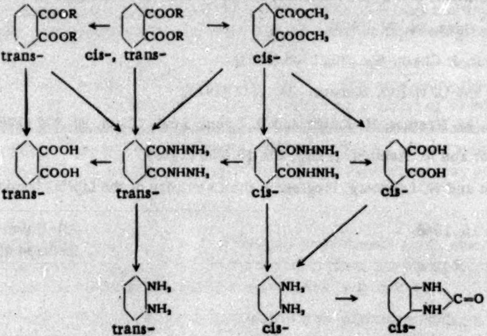
## III. CIS-1,2-DIAMINOCYCLOHEXANE

V. G. Iashunskii

It has been shown earlier [1] that "Complexon-IV" is trans-1,2-diaminocyclohexane-N,N'-tetraacetic acid, and it is obtained by the condensation of trans-1,2-diaminocyclohexane with monochloroacetic acid. It seemed of interest to synthesize the cis-isomer of this Complexon.

Until recently, however, there has been no mention in the literature of cis-1,2-diaminocyclohexane from which this Complexon could be obtained. At the time of completion of the present work a short communication [2] appeared, in which mention was made of the preparation of cis-1,2-diaminocyclohexane by degradation of cis-hexahydrobenzimidazolone.

The present communication describes the synthesis of cis-1,2-diaminocyclohexane by means of the Curtius reaction (by a scheme analogous to that for the preparation of the trans-isomer of this diamine [1]), and the Schmidt reaction.



In conformity with the data in the literature [4] the product of hydrogenation of diethyl (or dimethyl) phthalate over Raney nickel, from which we have previously prepared the dihydrazide of cis-1,2-cyclohexanedicarboxylic acid and subsequently by a Curtius degradation, trans-1,2-diaminocyclohexane, is a mixture of cis- and trans-1,2-cyclohexanedicarboxylic acids. Hence, in one of these stages (preparation of the dihydrazide or the Curtius reaction) cis-trans isomerization takes place. We succeeded in showing that this isomerization takes place on boiling the esters with hydrazine hydrate, and the dihydrazide formed, with m. p. 229-231°, has the trans-configuration. On hydrolysis it yielded trans-1,2-cyclohexanedicarboxylic acid. The configuration of the dihydrazide obtained was confirmed also by comparing it with a sample of the dihydrazide prepared by the interaction of diethyl trans-1,2-cyclohexanedicarboxylate with hydrazine hydrate.

Dimethyl cis-1,2-cyclohexanedicarboxylate under the same conditions, and also on carrying out the reaction in alcoholic solution at 120° in a sealed ampoule, is converted entirely to the trans-dihydrazide.

An example of a similar rearrangement is described in the literature [5]: under analogous conditions the corresponding trans-dihydrazide was obtained from the diester of cis-3,4-thiophanedicarboxylic acid.

cis-1,2-Cyclohexanedicarboxylic acid dihydrazide of m. p. 123-124.5° was prepared by reacting dimethyl cis-1,2-cyclohexanedicarboxylate with hydrazine hydrate in methyl alcohol at room temperature. Hydrolysis of this hydrazide with hydrochloric acid gave cis-1,2-cyclohexanedicarboxylic acid. On heating the cis-dihydrazide above its melting point it solidifies and melts again at 228.5-229.5°, i.e., it isomerizes to the trans-dihydrazide.

The cis-dihydrazide was subjected to the Curtius degradation whereby, without isolation of the intermediate diazine and diurethane, the diamine was obtained successfully, the dihydrochloride, dibenzoyl, diacetyl and dibenzenesulfonyl derivatives of which differed from the corresponding derivatives of the trans-diamine, giving mixed melting point depressions. On reacting with phosgene, cis-hexahydrobenzimidazolone was isolated. All this provides an adequate basis for considering that the diamine obtained has the cis-configuration. Thus, our results confirm the statement in the literature [6] that cis-trans isomerization does not occur in the Curtius reaction.

We also synthesized cis-1,2-diaminocyclohexane directly from cis-1,2-cyclohexanedicarboxylic acid by the Schmidt reaction. Here, as in the Curtius rearrangement, the configuration of the original compound is preserved. The reaction was carried out in two ways: a) by treating the cis-acid with a chloroform solution of hydrazoic acid in the presence of conc. $H_2SO_4$ and b) by adding dry sodium azide to a mixture of a benzene solution of the cis-acid and conc. $H_2SO_4$. In both cases, after steam distilling the base, cis-1,2-diaminocyclohexane dihydrochloride was obtained.

## EXPERIMENTAL

Diethyl trans-1,2-cyclohexanedicarboxylate (b. p. 127-128° at 7 mm, $n^{25}D$ 1.4482) and diethyl cis-1,2-cyclohexanedicarboxylate (b. p. 136-137.5° at 10 mm, $n^{25}D$ 1.4500) were obtained from the product of hydrogenation of diethyl phthalate over Raney nickel [4]. The dimethyl ester of the cis-acid was prepared by the same method and also from the butadiene-maleic anhydride adduct [7].

Reaction of the 1,2-cyclohexanedicarboxylic esters with hydrazine hydrate. 11.4 g of diethyl trans-1,2-cyclohexanedicarboxylate was added over a period of 1 hour to 12.5 g of 100% hydrazine hydrate at its boiling point. The mixture was heated a further 16 hours at 130° to form a solid, white mass, which was soluble in hot water. The liquid was separated from the crystals that separated on cooling and after recrystallizing from water, 8.2 g of trans-1,2-cyclohexanedicarboxylic acid dihydrazide, with m. p. 229-231° (with rapid heating of the capillary tube), was obtained.

Diethyl cis-1,2-cyclohexanedicarboxylate gave with hydrazine hydrate under the same conditions, a dihydrazide with m. p. 227.5-228.5°. A mixed melting point with the trans-dihydrazide gave no depression. Small quantities of the trans-dihydrazide and of the original ester were isolated from the mother liquor. Similar results were obtained with the dimethyl ester.

A mixture of 5 g of the cis-dimethyl ester, 5 g of hydrazine hydrate and 5 ml of absolute methyl alcohol were heated in a sealed tube at 115-120° for 4 hours. Only the trans-dihydrazide of m. p. 229-230.5° was obtained on working up the reaction mixture. On heating the trans-dihydrazide with concentrated hydrochloric acid, trans-1,2-cyclohexanedicarboxylic acid of m. p. 219.5-220.5° (from 25% aqueous acetone) was obtained.

cis-1,2-Cyclohexanedicarboxylic acid dihydrazide. A mixture of 30 g of dimethyl cis-1,2-cyclohexanedicarboxylate, 37.5 g of hydrazine hydrate and 50 ml of methyl alcohol was left to stand for a week at room temperature. The reaction mixture was then evaporated in vacuo (water-pump) at a temperature not above 50°. The residue was pressed out on a filter and washed with methyl alcohol and ether. After a two-fold recrystallization from absolute ethyl alcohol 18.85 g of the cis-dihydrazide, of m. p. 123-124.5°, was obtained.

Found %: N 27.91. $C_8H_{16}O_2N_4$. Calculated %: N 27.98.

On heating with concentrated hydrochloric acid this hydrazide gave cis-1,2-cyclohexanedicarboxylic acid of m. p. 189.5-190.5° (from water).

A small quantity of the cis-dihydrazide was heated above its melting point: at about 130° the material solidified and melted again at 215-220°. After recrystallizing from water it had m. p. 227.5-229.5°. A mixed melting point with the trans-dihydrazide gave no depression.

cis-1,2-Diaminocyclohexane. 7.5 g of the cis-dihydrazide was added with stirring and cooling to 26 ml of 10% hydrochloric acid. 30 ml of ether was then added and a solution of 5.32 g of sodium nitrite in 12 ml of water was added gradually at such a rate that the temperature of the mixture remained within the limits of 18 to 20°. After stirring at this temperature for 10 minutes the upper layer was separated off and the aqueous layer was extracted twice with 20 ml of ether. The combined ethereal extracts were dried for a short time over fused calcium chloride, filtered and mixed with 40 ml of absolute ether. The ether was slowly distilled from the resulting solution at 65-70° (in steam). The residue was refluxed for 1 hour, 36 g of potassium hydroxide and 100 ml of methyl alcohol were added and refluxing was continued for a further 2 hours on an oil bath at 120-130°. The reaction mixture was distilled with superheated steam. The distillate was acidified with hydrochloric acid (about 14 ml of 10% HCl) and evaporated to dryness on the water bath, yielding 4.2 g of crude cis-1,2-diaminocyclohexane dihydrochloride.

100 ml of a freshly prepared 2 N solution of hydrazoic acid in chloroform was added to a mixture of 13.5 g of cis-1,2-cyclohexanedicarboxylic acid, of m. p. 189-190.5°, prepared by saponification of the dimethyl ester, and 26 ml of conc. $H_2SO_4$ at 40°, with stirring. Stirring was continued at this temperature for 16 hours, after which the mixture was poured onto ice and the aqueous layer was steam distilled after being made alkaline. After evaporation of the acidified distillate, 3.5 g of the cis-diamine dihydrochloride was obtained.

6.5 g of sodium azide was added in small portions over a period of 1 hour to a mixture of 6 g of the cis-acid, 14 ml of conc. $H_2SO_4$ and 50 ml of chloroform at 40°; after stirring at this temperature for 10 hours the reaction mixture was treated as described above and 1.2 g of the cis-diamine dihydrochloride was obtained. The free base was isolated by ether extraction after treatment of a concentrated aqueous solution of cis-1,2-diaminocyclohexane dihydrochloride with solid alkali. It was redistilled at 92-93° and 18 mm.

cis-1,2-Diaminocyclohexane dihydrochloride was prepared by treatment of the base with alcoholic hydrogen chloride solution. M. p. 307-310°.

Found %: C 38.44; H 8.72; Cl 37.79. $C_6H_{14}N_2 \cdot 2HCl$. Calculated %: C 38.52; H 8.62; Cl 37.91.

The remaining derivatives were prepared both from the free base and from the unpurified dihydrochloride isolated directly from the Curtius and Schmidt reactions.

Dibenzoyl derivative (Schotten-Baumann method), m. p. 186.5-187° (from alcohol).

Found %: C 74.45; H 6.92; N 8.72. $C_{20}H_{22}O_2N_2$. Calculated %: C 74.50; H 6.88; N 8.69.

Diacetyl derivative — an oily product.

Dibenzenesulfonate, m. p. 165-166° (from 40% alcohol).

Found %: N 7.09. $C_{18}H_{22}O_4N_2S_2$. Calculated %: N 7.10.

Dipicrate, m. p. 260° (decomp., from water).

Found %: N 19.27. $C_6H_{14}N_2 \cdot 2C_6H_3O_7N_3$. Calculated %: N 19.71.

In the communication [2] mentioned above the following constants for cis-1,2-diaminocyclohexane are given: free base, b. p. 93-95° at 20 mm; dihydrochloride, m. p. about 270°; dibenzoyl derivative, m. p. 184-185°; dipicrate, m. p. 160° (decomp.).

cis-Hexahydrobenzimidazolone. 0.9 g of cis-1,2-diaminocyclohexane in 8 ml of 10% potassium hydroxide solution was treated, with vigorous cooling, with 8 ml of an 16% toluene solution of phosgene. The reaction mixture was evaporated to dryness and the residue was extracted with hot benzene. After removal of the benzene a white powder remained, which after recrystallizing from acetone had m. p. 147-148°. According to the literature: m. p. 147-149° [3].

## SUMMARY

1. It has been established that by reacting hydrazine hydrate with esters of cis-and trans-1,2-cyclohexanedicarboxylic acid, by heating to 120-130°, only trans-1,2-cyclohexanedicarboxylic acid dihydrazide is obtained. The cis-dihydrazide is obtained by carrying out the reaction at room temperature.

2. cis-1,2-Diaminocyclohexane, which was characterized by a number of derivatives, was synthesized by the Curtius reaction from cis-1,2-cyclohexanedicarboxylic acid dihydrazide. The cis-diamine was prepared also by the Schmidt reaction from cis-1,2-cyclohexanedicarboxylic acid.

3. The statement in the literature that cis-trans isomerization does not occur in the preparation of amines by the Curtius and Schmidt reactions has been confirmed.

## LITERATURE CITED

[1] V. G. Iashunskii and M. N. Shchukina, J. Gen. Chem. 28, 230 (1958).*

[2] F. Winternitz and J. Condamines, Bull. Soc. Chim. 750 (1956).

[3] J. P. English, R. C. Clapp, Q. P. Cole, J. F. Halverstadt, J. O. Lampen and R. O. Roblin, J. Am. Chem. Soc. 67, 301 (1945).

[4] C. C. Price and M. Schwarcz, J. Am. Chem. Soc. 62, 2891 (1940).

[5] B. R. Baker, S. Berenstein and S. R. Safir, J. Org. Ch. 12, 155 (1947).

[6] J. H. Müller, M. N. Donin, W. E. Behnke and K. Hofmann, J. Am. Chem. Soc. 73, 2487 (1951).

[7] Synthetic Organic Preparations, IV, 252 (1953).**

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# RESEARCH IN THE FIELD OF SUBSTITUTED PHENYLOSAZONES AND PHENYLHYDRAZONES

## II. SOME NEW NITROPHENYLOSAZONES OF DIHYDROXYTARTARIC ACID

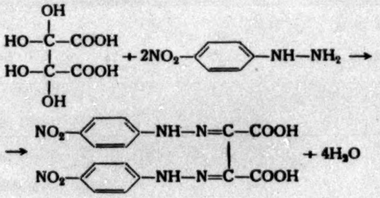
N. V. Chugreeva

It is evident from numerous sources in the literature that phenylosazones and phenylhydrazones (as well as their nitro and halogen derivatives) of compounds containing carbonyl groups have been prepared and used only for the identification of these compounds up to the present time. For this purpose such characteristics as melting point, crystalline form, color, and solubility in organic compounds are most often used.

In a number of papers describing the methods of preparation and properties of some nitrophenylhydrazones and nitrophenylosazones it is pointed out that the latter are capable of dissolving in alkali with a change in color, thus displaying indicator properties to some degree [1-6].

These facts led us* to synthesize and examine not only the phenylhydrazones and osazones already described in the literature but also a number of other compounds, the properties of which were not known. This paper is concerned with some dihydroxytartaric acid nitrophenylosazones, the structure of which suggests that they are capable of indicator action.

There are a number of methods for synthesizing nitrophenylosazones and nitrophenylhydrazones. For our purpose we utilized the direct reaction of the carbonyl-containing compounds with nitro derivatives of phenylhydrazine, which proceeds (in the case of dihydroxytartaric acid and p-nitrophenylhydrazine) according to the following scheme:



## EXPERIMENTAL

Dihydroxytartaric acid p-nitrophenylosazone. For the preparation of this osazone we did not actually start with the relatively unstable hydrate of dihydroxytartaric acid but with its disodium salt, using the method described by Kul'berg [7] for unsubstituted phenylosazones, with the introduction of slight modifications to the method. With the object of improving the purity of the product without decreasing its yield, we filtered the precipitate using a Büchner funnel attached to an aspirator and washed (at least 6 times) with small portions of distilled water slightly acidified with hydrochloric acid; this procedure was followed by at least the same number of washings with cooled aqueous (50%) alcohol solution (instead of washing with acetone as recommended previously).

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* This work was carried out under the guidance of Professor L. M. Kul'berg.

Found % N 20.11, 20.21. $C_{16}H_{12}O_8N_6$. Calculated % N 20.18.

Dihydroxytartaric acid p-nitrophenylosazone is a red, crystalline substance (with a slight brownish tinge), melting with decomposition at 234.5-235° (from alcohol). It is practically insoluble in cold and only slightly soluble in hot water, benzene, chloroform and carbon tetrachloride; it dissolves rather more readily in ethyl alcohol and acetone and is quite soluble in methyl alcohol. Saturated aqueous solutions are pale yellow in color, and alcoholic solutions are yellow-orange. The color of the chloroform solution is close to that of an alcoholic solution of the same concentration. Solutions in benzene and carbon tetrachloride are pale orange with a pink tinge.

When added to a solution of sodium or potassium hydroxide (0.5N or above), crystalline dihydroxytartaric acid p-nitrophenylosazone dissolves readily and gives a blue color, showing that this osazone has indicator properties. Solutions of the osazone in water and in organic solvents behave in the same way, i.e., they turn blue or dark blue when they are added to alkaline solutions of the stated concentrations. The aqueous and alcoholic solutions are unstable and lose their indicator properties comparatively rapidly (storage period not more than 3 days). Solutions in other organic solvents (benzene, toluene, chloroform, carbon tetrachloride) are considerably more stable and can be kept for weeks or even months without loss of indicator properties. Dry dihydroxytartaric acid p-nitrophenylosazone is completely stable; samples of it tested immediately after preparation and 2 years after preparation are absolutely identical in properties.

By careful addition of concentrated (25%) ammonia solution to the crystalline p-nitrophenylosazone and subsequent removal of water and excess ammonia by heating on a boiling water bath, we obtained a reddish-brown substance — the ammonium salt of dihydroxytartaric acid p-nitrophenylosazone. An advantage of this salt over the corresponding osazone of the free acid is its better solubility in water at ordinary temperatures, which enables us to dispense with the use of alcohol in practical applications.

Dihydroxytartaric acid 2,4-dinitrophenylosazone. The synthesis of this substance was achieved by the scheme described above for dihydroxytartaric acid p-nitrophenylosazone. The 2,4-dinitrophenylosazone is rather more soluble in alcohol than the p-nitrophenylosazone, consequently the precipitate was washed initially with cooled distilled water (not less than 7-8 times, small portions) and finally (3-4 times) with cold aqueous ethyl alcohol (40%). The washed precipitate was pressed between sheets of filter paper, after which it was immediately transferred to an oven and dried at 105-110° to constant weight.

The ammonium salt of dihydroxytartaric acid 2,4-dinitrophenylosazone can be prepared easily by direct interaction of the crystalline osazone with concentrated ammonia solution. After the excess ammonia was evaporated off on a boiling water bath, a bright red crystalline product with a slight orange tinge remained. After it was dried to constant weight at 120-125°, the ammonium salt was unchanged in properties. M. p. 311-311.5° (decomp.). Analysis for nitrogen content showed that the product was the monoammonium salt.

Found % N 24.38. $C_{16}H_{13}O_{12}N_9$ (acid salt). Calculated % N 24.09. $C_{16}H_{16}O_{12}N_{10}$ (neutral salt). Calculated % N 25.92.

The 2,4-dinitrophenylosazone of the free acid is a dark yellow substance. It can be kept in the pure state only in complete absence of gaseous ammonia, which is ordinarily present in the laboratory; in the presence of gaseous ammonia the ammonium salt is gradually formed. It was not possible to determine the melting point of the 2,4-dinitrophenylosazone of the free acid accurately because of its rapid conversion to the ammonium salt.

With respect to solubility in water and organic solvents, the dinitrophenylosazone of the free acid is similar to dihydroxytartaric acid p-nitrophenylosazone described above. Its solutions are yellow in color in various shades.

On adding the crystalline osazone to sodium or potassium hydroxide solutions (0.5 N or above) they dissolve readily giving a light violet color. On lowering the hydroxyl ion concentration the color changes to light yellow. Similar results were obtained with aqueous and alcoholic solutions.

The ammonium salt of dihydroxytartaric acid 2,4-dinitrophenylosazone is rather more soluble in water than the osazone of the free acid; even at room temperature the solutions are colored a fairly bright yellow. Addition of sodium or potassium hydroxide to such solutions causes a color change to light violet. The dry salt also gives a light violet color to sodium and potassium hydroxide solutions of the above-mentioned concentrations. Aqueous and alcoholic solutions of free dihydroxytartaric acid dinitrophenylosazone and its ammonium salt are considerably more stable than similar solutions of dihydroxytartaric acid p-nitrophenylosazone. They can be kept without loss of indicator properties for several months. The dry ammonium salt is completely stable and does not alter its chemicoanalytical nature on storage.

Dihydroxytartaric acid o-nitrophenylosazone was prepared in a similar manner to that described above for the p-nitro- and 2,4-dinitrophenylosazones.

The pure product was obtained by recrystallizing from boiling ethyl alcohol (96%) with subsequent cooling to 10-15°. On drying in air it is not subject to the action of gaseous ammonia and the ammonium salt can be formed only by treatment with ammonium hydroxide solution as described above for dihydroxytartaric acid p-nitrophenylosazone.

Found %: N 20.30, 20.15. $C_{16}H_{12}O_8N_6$. Calculated %: N 20.18.

Dihydroxytartaric acid o-nitrophenylosazone is an orange colored crystalline substance with a slightly reddish tinge, melting with decomposition at 228°. It is practically insoluble in water. Its solubility in boiling water and organic solvents is of approximately the same order as for the p-nitrophenylosazone. Saturated aqueous solutions have a dull orange-pink color which is unchanged on addition of solutions of alkali hydroxides and carbonates or ammonia. Alcoholic solutions are colored a light orange. On adding them to distilled water or to alkaline solutions they give a dull orange-pink color, on acidification the solutions become pale yellow. The dry product is completely stable; as regards the aqueous and alcoholic solutions, they are more stable than solutions of the p-nitrophenylosazone; their indicator properties do not change for several weeks.

Dihydroxytartaric acid m-nitrophenylosazone was also synthesized in a similar manner to the nitrophenylosazones described above. It was purified by recrystallizing from hot ethyl alcohol (96%).

Found %: N 20.29, 20.22. $C_{16}H_{12}O_8N_6$. Calculated %: N 20.18.

Dihydroxytartaric acid m-nitrophenylosazone is a crystalline substance, bright yellow in color with a slight orange tinge; it melts at 227.5-228°. Its solubility in water and in organic solvents is similar to that of the nitrophenylosazones described above. The solutions are pale yellow in color and do not change under the action of alkalis (of concentrations up to 6 N) or of acids. On keeping the solutions for several months their properties do not change; the dry material is also completely stable.

## SUMMARY

The p-nitrophenylosazone, o-nitrophenylosazone, m-nitrophenylosazone and 2,4-dinitrophenylosazone of dihydroxytartaric acid and also the monoammonium salt of dihydroxytartaric acid 2,4-dinitrophenylosazone, not described in the literature, have been synthesized. The compounds obtained were suitably characterized and it was found that all these nitroderivatives, with the exception of dihydroxytartaric acid m-nitrophenylosazone, are capable of undergoing indicator changes.

## LITERATURE CITED

[1] Th. Kurtius and G. M. Dedichen, J. pr. Ch. 50, 241 (1894).

[2] E. Hyde, Ber. 32, 1813 (1899).

[3] F. Feist, Ber. 33, 2099 (1900).

[4] G. V. Chelintsev, J. Gen. Chem. 14, 941 (1944).

[5] M. Ragno, Gazz. 75, 175 (1945).

[6] G. R. Lappin and L C. Clark, Anal. Chem. III, 23, 514 (1951).

[7] L. M. Kul'berg, Synthetic Organic Reagents, State Chemical Press 104 (1947).*

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# INVESTIGATION OF THE RELATIVE REACTIVITY OF THE HYDROXYL GROUPS OF CELLULOSE*

## VII. ON THE DISTRIBUTION OF METHOXYL GROUPS IN PARTIALLY METHYLATED CELLULOSE, OBTAINED FROM CELLULOSE TREATED WITH SODIUM ISOAMYLATE

V. Derevitskaia, M. Prokof'eva and Z. Rogovin

From the supposition that there is in the cellulose molecule one hydroxyl group with increased acid properties, the formation of a cellulose alcoholate might be expected not only by the direct action of metallic sodium but also by means of an exchange reaction with an alcoholate of a simple alcohol.

Rassow and Wadewitz [1] were first to attempt to prepare the Na-alcoholate of cellulose in this way. They treated cellulose with solutions of sodium methylate or ethylate in the corresponding alcohols. After the cellulose was treated for 4 hours, the concentrations in the solutions were unchanged. This indicates that under the conditions chosen the Na-alcoholate of cellulose is not formed.

The failure of the above investigators can obviously be explained by the fact that they carried out the reaction in a large excess of the alcohol, which cannot but lead to alcoholysis of the cellulose alcoholate formed. In order to avoid this, one must use Na-alcoholate dissolved in an inert organic solvent. Later [2], by an exchange reaction with thallium alcoholate, cellulose Tl-alcoholate was obtained. This reaction was used for investigation of the structure of cellulose preparations. The cellulose Tl-alcoholate obtained had $\gamma \approx 100$.

In the present work the Na-derivative of cellulose was prepared by the action of sodium isoamylate on cellulose in an inert solvent.

The starting material used for the preparation of the cellulose Na-derivative was cotton cellulose treated with alkali and then by the solvent-displacement method to give an "inclusion" cellulose [3]. The cellulose was treated with a solution of Na-isoamylate [4] in p-xylene, with exclusion of atmospheric moisture and $CO_2$. The product obtained was washed free from excess Na-isoamylate with xylene, to neutral reaction of the xylene washings. The sodium content of the cellulose Na-derivative was determined by titration [5]. The cellulose Na-derivative obtained had $\gamma$ 250-260.

It should be noted that the preliminary treatment of the cellulose plays a significant role in the successful conduct of this reaction. Only cellulose regenerated from alkaline cellulose with subsequent inclusion displays sufficient reactivity for this reaction. Preparations of freshly spun viscose rayon and viscose rayon included with benzene without previous swelling in alkali, after treatment with a solution of sodium isoamylate in xylene and subsequent isolation, do not contain sodium.

For the purpose of studying the relative reactivity of the hydroxyl groups of cellulose, samples of the Na-derivative of cellulose of $\gamma \approx 100$-200 were prepared (Table 1).

Two methods were used for preparing the Na-derivative of cellulose of $\gamma \approx 100$.

a) By the action of one mole of sodium isoamylate per mole of cellulose with subsequent removal of

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* The 66th communication in the series "Investigation of the structure and properties of cellulose."

TABLE 1

| Sample No. | Quantity of Na-isoamylate (in moles per mole of cellulose) | Solvent used for washing the product | $\gamma$ Na-derivative of cellulose | $\gamma$ Methyl cellulose |
|---|---|---|---|---|
| 1 | 7 | Benzene | 262 | – |
| 2 | 7 | | 257 | 83.5 |
| 3 | 7 | | – | 130 |
| 4 | 7 | | – | 131 |
| 5 | 7 | Isobutyl alcohol | 71 | 72.5 |
| 6 | 7 | | 83.3 | 81.3 |
| 7 | 7 | | 83.3 | 77 |
| 8 | 7 | | 72 | 70.5 |
| 9 | 0.87 | Benzene | 85 | 55 |
| 10 | 1 | | 100 | 89 |
| 11 | 1.23 | | 122 | – |
| 12 | 1.3 | | 130 | 99.5 |
| 13 | 2 | | 199 | 106 |
| 14 | 2 | | 199 | 50.5 |

TABLE 2

| Sample No. (see Table 1) | $\gamma$, Methyl cellulose | $\gamma$, Trityl ether of methyl cellulose | Number of $OCH_3$ groups per $C_6$ | Z* |
|---|---|---|---|---|
| 6 | 81.3 | 88 | 12 | 2.9 |
| 7 | 77 | 89 | 11 | 3 |
| 8 | 70.5 | 93 | 7 | 4.6 |
| 9 | 55 | 95 | 5 | 5 |
| 10 | 89 | 85 | 15 | 2.3 |
| 12 | 99.5 | 80 | 20 | 2 |
| 13 | 106 | 78 | 22 | 1.9 |

adsorbed isoamylate by washing with xylene. In this case the reaction medium (xylene) and the first portion of xylene used for washing had a neutral reaction, i.e., the sodium was completely combined with the cellulose (Table 1).

b) By washing a cellulose alcoholate of $\gamma$ 250-260 with dry isobutyl alcohol to neutral reaction of the alcohol washings. Under these conditions an alcoholate with a value of $\gamma$ near to 100 was always obtained, as in the case of washing the cellulose trialcoholate, prepared from alkaline cellulose in a medium of liquid ammonia, with isobutyl alcohol.

The alcoholate obtained was then methylated with methyl iodide. For determination of the nature of the methoxyl group distribution in the methyl cellulose obtained the number of free, primary hydroxyl groups was determined by tritylation. The results are presented in Table 2.

As is seen from the data in Table 2 the average number of methoxyl groups combined per secondary carbon atom exceeds by 2-5 times the number of methoxyl groups per primary carbon atom. The distribution of methoxyl groups in methyl cellulose is practically independent of the method of preparation of the Na-derivative of cellulose subjected to methylation.

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* Z is the ratio of the average number of methoxyl groups combining per secondary carbon atom to the number of methoxyl groups per primary carbon atom.

## EXPERIMENTAL

Cotton [6] was used as starting material. Scoured, air-dried cotton was treated [3] with 10% of alkali solution at 5° for 3 hours, the swollen mass was then treated with an equal quantity of 2% alkali solution and after 30 minutes the cotton was filtered off, washed with water, 1% acetic acid and again with water to neutral reaction. Water was displaced from the cotton by methanol, for this purpose the cotton, after water had been squeezed out, was stirred in 1 liter of methanol. After 15 minutes the cotton was squeezed out and steeped in a fresh portion of methanol followed by treatment with a further two fresh portions of dry methanol for 30 minutes each time. Methanol was then rapidly squeezed out from the cotton which was then kept in absolute benzene.

Sodium isoamylate was prepared by the method of Bruhl [4]. A weighed amount of sodium was melted under boiling p-xylene and a fine suspension of sodium in p-xylene was obtained by vigorous shaking. The calculated quantity of isoamyl alcohol was added to the suspension after cooling, the apparatus being protected from moisture and $CO_2$. By this means Na-isoamylate of high reactivity, free from alcohol of crystallization, was obtained.

A weighed amount of cellulose, previously squeezed out rapidly from benzene, was added to the solution of Na-isoamylate in p-xylene heated to 66-70° (placed in an apparatus fitted with a reflux condenser, stirrer and soda-lime tube). The reaction was carried out for 1 hour at 70° (with continuous stirring) and then for some time at room temperature: for the preparation of the Na-derivative of cellulose of $\gamma \approx 100$ this period was 1 hour, for $\gamma \approx 200 - 3$ hours, and for treatment of cellulose with a large excess of Na-isoamylate – 24 hours. The Na-derivative of cellulose obtained was filtered off rapidly and washed with absolute xylene or isobutyl alcohol, in a flask with a ground-glass stopper, to neutral reaction of the washing liquid. The quantity of combined sodium was determined by titration with 0.01N $H_2SO_4$ [5].

The Na-derivative of cellulose was methylated with methyl iodide (26 moles per mole of cellulose) in the same apparatus at 42° or in a sealed ampoule at 100° for 3.5 hours. For the determination of methoxyl groups, tritylation of methyl cellulose and analysis of the trityl ether, previously published methods were used [6].

## SUMMARY

1. In the reaction between cellulose and Na-isoamylate and subsequent methylation, the secondary hydroxyl groups possess high reactivity.

2. The average number of methoxyl groups combining per secondary carbon atom is approximately 2-5 times greater than the number of methoxyl groups per primary carbon atom.

## LITERATURE CITED

[1] B. Rassow and M. Wadewitz, J. pr. Ch. 106, 266, 272 (1923).

[2] C. Harris and C. Parves, Paper Trade J. 110, 29 (1940).

[3] Assaf, Haas and Purves, J. Am. Chem. Soc. 66, 59 (1944).

[4] J. Brühl, Ber. 37, 2067 (1904).

[5] M. Ginsberg and Z. Rogovin, Exchange of Technical Experience, Synthetic Fiber, Collection 2, State Light Industry Press 52 (1952).*

[6] V. Derevitskaia, Iu. Kozlova and Z. Rogovin, J. Gen. Chem. 24, 1466 (1956).**

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# THYROID GLAND HORMONES AND THEIR ANALOGS

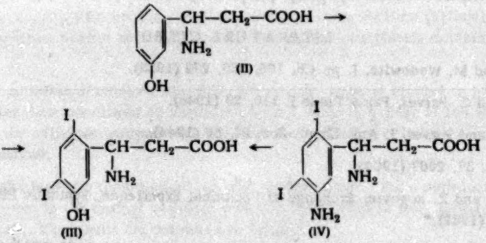
## II. SYNTHESIS OF ISOMERS OF BETAZINE

N. N. Suvorov and A. A. Dudinskaia

β-Diiodotyrosine, synthesized by one of us with V. M. Rodionov and V. G. Avramenko [1], which possesses high antithyrotropic (antithyroidal) activity, finds application in medicine for the treatment of thyrotoxicoses, under the name of "Betazine." β-Diiodotyrosine is β-(4-hydroxy-3,5-diiodophenyl)-β-alanine. For the purpose of studying the relationship between antithyroidal activity and chemical structure it was not without interest to synthesize isomers with the phenolic hydroxyl in positions other than that in Betazine.

We have prepared the ortho analog of Betazine, β-(2-hydroxy-3,5-diiodophenyl)-β-alanine, by iodination of β-(2-hydroxyphenyl)-β-alanine which was synthesized by Posner [2] by reacting coumarin with hydroxylamine. It should be noted that demethylation of β-(2-methoxyphenyl)-β-alanine by boiling with hydrobromic acid according to the method developed for β-(4-methoxyphenyl)-β-alanine [1] does not lead to the hydroxyamino acid: on demethylation coumarin is formed with elimination of a molecule of ammonia.

For the synthesis of the meta isomer of Betazine β-(3-hydroxyphenyl)-β-alanine (II), prepared from m-hydroxybenzaldehyde by the V. M. Rodionov reaction, was subjected to iodination with iodine monochloride. It is interesting to note that even in the presence of a large excess of iodinating agent, not the tri- but the diiodo derivative is formed. On the basis of steric considerations the structure β-(3-hydroxy-4,6-diiodophenyl)-β-alanine (III) was ascribed to the latter, this being further confirmed by its preparation through the diazo compound from β-(3-amino-4,6-diiodophenyl)-β-alanine (IV), the structure of which we have proved conclusively [3].



It should be pointed out that the American chemist Jackson [4] recently came to a similar conclusion for a series of amino acids, showing by a rather complicated method, that on iodination of m-tyrosine, β-(3-hydroxy-4,6-diiodophenyl)-alanine is formed.

Information on the physiological activity of the compounds prepared by us will be published elsewhere.

### EXPERIMENTAL

β-(2-Hydroxy-3,5-diiodophenyl)-β-alanine (I). β-(2-Hydroxyphenyl)-β-alanine was prepared by the method of Posner [2]. Yield 60%. M. p. 213.5° (decomp.). To a solution of 3 g of this amino acid in a mixture of 0.6 ml of concentrated hydrochloric acid and 51 ml of water, 5.93 g of iodine monochloride in 12 ml of hydrochloric acid (1:1) was added dropwise at 50°. Heating was continued for a further 2 hours, after which excess iodine was removed with sodium bisulfite. The precipitate that separated (5.6 g) was filtered off and washed with acetone and ether. It consisted of the hydrochloride of of β-(2-hydroxy-3,5-diiodophenyl)-β-alanine.

Found %: Cl (ionic) 7.65, 7.68. $C_9H_9O_3NI_2 \cdot HCl$. Calculated %: Cl (ionic) 7.56.

From a solution of 5.6 g of this hydrochloride in 120 ml of water and 2.1 ml of concentrated hydrochloric acid, free β-(2-hydroxy-3,5-diiodophenyl)-β-alanine (3.6 g) was precipitated (by addition of a saturated solution of sodium acetate at 80°). M. p. 178.5-179° (decomp.).

Found %: I 57.98. $C_9H_9O_3NI_2$. Calculated %: I 58.65.

2-Methoxycinnamic acid. A mixture of 50 g of 2-methoxybenzaldehyde [5], 50 g of malonic acid, 50 ml of dry pyridine and 5 ml of piperidine was refluxed for 4 hours. The reaction mixture was then poured into 500 ml of 12% hydrochloric acid. The precipitate that separated was filtered off, washed with water and crystallized from alcohol. Yield 53 g (81%). M. p. 183-184°. According to the literature [6]: m. p. from 182 to 186°.

β-(2-Methoxyphenyl)-β-alanine was prepared by the following modification of Posner's reaction. A hot solution of 10.5 g of hydroxylamine hydrochloride in 4.2 ml of water was added in one lot to a hot solution of sodium butylate (from 3.48 g of metallic sodium and 70 ml of anhydrous n-butyl alcohol), and the mixture was cooled immediately. The sodium chloride that precipitated was filtered off and to the filtrate was added 5 g of 2-methoxycinnamic acid and the mixture was boiled under reflux for 10 hours. The amino acid was then extracted with water, the water was distilled off in vacuo to dryness and the resinous residue was dissolved in 35 ml of absolute alcohol. The alcoholic solution was treated with activated charcoal, concentrated in vacuo to a small volume and the amino acid was precipitated by the addition of absolute ether. After washing the precipitate with ether 0.65 g of β-(2-methoxyphenyl)-β-alanine was obtained. M. p. 209-210° (decomp.). Posner [7] gives m. p. 209-210°.

Found %: C 61.74, 61.82; H 6.53, 6.69; N 6.76. $C_{10}H_{13}O_3N$. Calculated %: C 61.53; H 6.66; N 7.18.

Demethylation of β-(2-methoxyphenyl)-β-alanine. A solution of 0.37 g of this amino acid in 5 ml of 48% hydrobromic acid was refluxed for 3.5 hours. The hydrobromic acid was distilled off to dryness in vacuo. Addition of 3 ml of water gave a precipitate (0.16 g). After two recrystallizations from water, its melting point was 69-70°; no melting point depression was given on mixing with an authentic sample of coumarin.

β-(3-Hydroxyphenyl)-β-alanine (II). m-Hydroxybenzaldehyde was prepared according to the directions of Woodward [8]. 25 g of this aldehyde, 24 g of malonic acid, 37.5 g of ammonium acetate and 50 ml of n-butyl alcohol were refluxed for 2.5 hours. The precipitate formed was filtered off from the still hot solution and washed with alcohol and ether. Yield 19.5 g (53%). M. p. 222-223° (decomp.). Posner [9] gives m. p. 235-236°.

Found %: N 7.69. $C_9H_{11}O_3N$. Calculated %: N 7.73.

The amino acid obtained was used immediately for iodination.

3.2 g of m-hydroxycinnamic acid of m. p. 190-191° was isolated from the butanol filtrate.

β-(3-Hydroxy-4,6-diiodophenyl)-β-alanine (III). To a solution of 8.8 g of β-(3-hydroxyphenyl)-β-alanine in a mixture of 1.8 ml of conc. HCl and 150 ml of water, a solution of 17.4 g of iodine monochloride in 17 ml of conc. HCl and 17 ml of water was added dropwise at 60° over a period of 30 minutes. Then, after heating the reaction mixture at this temperature for a further 2 hours, 6 ml of a saturated solution of sodium bisulfite was added. The solution was treated with activated charcoal and β-(3-hydroxy-4,6-diiodophenyl)-β-alanine was isolated by adding saturated sodium acetate solution until the mixture was no longer acid to Congo. Yield 16.8 g (80%). After purifying through the difficultly soluble sulfate the melting point was 212-213° (decomp.).

Found %: N 3.13, 3.08; I 58.58, 58.48. $C_9H_9O_3NI_2$. Calculated %: N 3.23; I 58.65.

The O,N-diacetyl derivative was obtained by heating 0.79 g of this amino acid with 7.9 ml of acetic anhydride and 0.2 ml conc. $H_2SO_4$ for 6 hours at 50-55° with subsequent decomposition of the reaction mixture with 80 ml of ice water. M. p. 235-235.5° (decomp., from a 1:2 mixture of alcohol and water).

Found %: I 49.41. $C_{13}H_{13}O_4NI_2$. Calculated %: I 49.12.

N-Acetyl-β-(3-hydroxy-4,6-diiodophenyl)-β-alanine was prepared by heating a solution of the O,N-diacetyl derivative (0.5 g) in 24 ml of 2N sodium hydroxide for 3.5 hours at 55-60° with subsequent acidification with dilute hydrochloric acid. M. p. 203.5-204.5° (decomp., from a mixture of alcohol and dichloroethane).

Found %: I 53.11. $C_{11}H_{11}O_4NI_2$. Calculated %: I 53.47.

Preparation of β-(3-hydroxy-4,6-diiodophenyl)-β-alanine (III) from β-(3-amino-4,6-diiodophenyl)-β-alanine (IV). To a solution of 4 g of (IV) in a mixture of 35 ml of conc. $H_2SO_4$ and 40 ml of water, a solution of 0.96 g of sodium nitrite in 7 ml of water was added dropwise at 0-5°. The reaction mixture was maintained at this temperature for 2 hours and was then poured into 40 ml of dilute sulfuric acid (1:1), heated to 135-140°. After heating for 30 minutes at this temperature the solution was cooled, whereby 3.5 g (71%) of the sulfate of β-(3-hydroxy-4,6-diiodophenyl)-β-alanine precipitated. M. p. 228° (decomp., from alcohol).

3.5 g of the sulfate was dissolved in a mixture of 73 ml of water and 27 ml of conc. HCl, the solution was heated to 60° and the free amino acid was precipitated by addition of a saturated solution of sodium acetate. Yield 2.31 g (58%). M. p. 213° (decomp.). No melting point depression was given in admixture with the amino acid prepared by iodination of β-(3-hydroxyphenyl)-β-alanine. The O,N-diacetyl derivatives of these amino acids were also identical.

## SUMMARY

1. For the purpose of studying the relationship between antithyrotropic (antithyroidal) activity and chemical structure β-(2-hydroxy-3,5-diiodophenyl)-β-alanine and β-(3-hydroxy-4,6-diiodophenyl)-β-alanine were synthesized, these being the ortho and meta isomers (respectively) of β-diiodotyrosine (Betazine).

2. It was found that on iodination of β-(3-hydroxyphenyl)-β-alanine with iodine monochloride not the triiodo – but the diiodo-substituted derivative – β-(3-hydroxy-4,6-diiodophenyl)-β-alanine is formed.

3. It is shown that boiling β-(2-methoxyphenyl)-β-alanine with hydrobromic acid leads to the formation of coumarin.

## LITERATURE CITED

[1] V. M. Rodionov, N. N. Suvorov, V. G. Avramenko and L. M. Morozovskaia, J. Gen. Chem. 27, 2234 (1957);* N. N. Suvorov, V. G. Avramenko and L. M. Morozovskaia, Authors' Certificate No. 104,779 (1956).

[2] T. Posner, Ber. 42, 2523 (1909).

[3] N. N. Suvorov, A. A. Dudinskaia and L. M. Morozovskaia, J. Gen. Chem. 28, 1374 (1958).*

[4] E. Jackson, J. Am. Chem. Soc. 77, 4860 (1955).

[5] C. Hell and A. Hofmann, Ber. 38, 1676 (1905).

[6] Beilst. X, 290.

[7] T. Posner, Lieb. Ann. 389, 59 (1912).

[8] Synthetic Organic Preparations, Collected Volume 3, 363 (1952) (Russian Translation of Organic Syntheses, Gilman-Blatt-Horning).

[9] T. Posner, Lieb. Ann. 389, 51 (1912).

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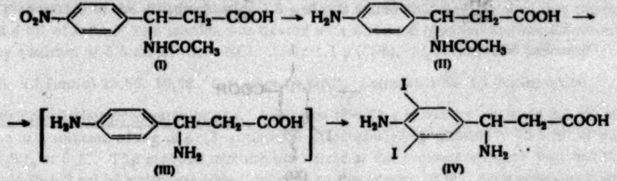
# THYROID GLAND HORMONES AND THEIR ANALOGS

## III. SYNTHESIS OF AMINO ANALOGS OF BETAZINE

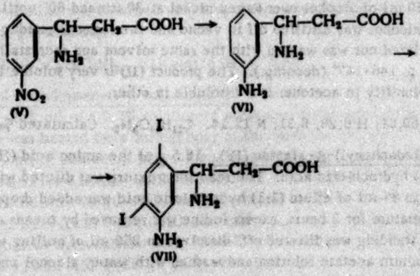
N. N. Suvorov, A. A. Dudinskaia and L. M. Morozovskaia

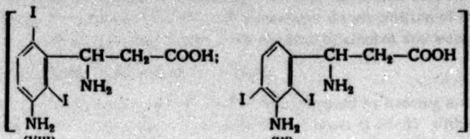
**For the purpose of studying the relationship between antithyrotropic (antithyroidal) activity and chemical structure we have synthesized β-(4-amino-3,5-diiodophenyl)- and β-(3-amino-4,6-diiodophenyl)-β-alanine, which are the amino analogs of β-diiodotyrosine (Betazine) [1] and its isomer, β-(3-hydroxy-4,6-diiodophenyl)-β-alanine [2].**

**We used as starting material for the synthesis of the 4-amino analog of Betazine, N-acetyl-β-4-nitrophenyl-β-alanine (I), previously prepared by one of us [3], which was hydrogenated over Raney nickel to β-4-amino-phenyl-β-N-acetylaminopropionic acid (II). The latter was hydrolyzed and the β-4-aminophenyl-β-alanine (III) formed was iodinated with iodine monochloride in dilute hydrochloric acid, without isolation in the pure state, with the formation of the required β-(4-amino-3,5-diiodophenyl)-β-alanine (IV).**


O₂N
CH—CH₂—COOH
NHCOCH₃
(I)
H₂N
CH—CH₂—COOH
NHCOCH₃
(II)
H₂N
CH—CH₂—COOH
NH₂
(III)
I
H₂N
CH—CH₂—COOH
I
NH₂
(IV)

**For the synthesis of β-(3-amino-4,6-diiodophenyl)-β-alanine (VII) the readily available β-3-nitrophenyl-β-alanine (V) was hydrogenated over Raney nickel and the β-3-aminophenyl-β-alanine (VI) obtained was iodinated with iodine monochloride.**

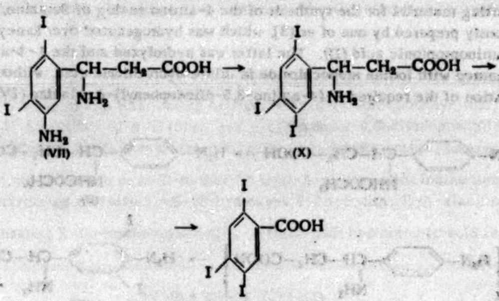

CH—CH₂—COOH
NH₂
NO₂
(V)
CH—CH₂—COOH
NH₂
NH₂
(VI)
I
CH—CH₂—COOH
NH₂
I
NH₂
(VII)



(VIII) (IX)

It is interesting to note that even in the presence of a large excess of iodine chloride it was not possible to prepare the triiodo derivative; evidently this is because an iodine atom cannot take up a position between the aromatic amino group and the β-alanine side chain [2]. Hence, we ascribed structure (VII) to the iodination product, rejecting structures (VIII) and (IX) as improbable.

Conclusive evidence of the structure of the diiodo derivative (VII) was obtained in the following way: the aromatic amino group was substituted by iodine through the diazo compound and the triiodoamino acid (X) obtained was oxidized with potassium permanganate to form a triiodobenzoic acid of m. p. 247-248°. The latter was shown to be identical with 2,4,5-triiodobenzoic acid, described by Wheeler and Johns [4], by direct comparison of the acids themselves and of the ethyl esters which we prepared.



(VII) (X) (XI)

Information on the physiological activity of the compounds prepared will be published elsewhere.

## EXPERIMENTAL

β-4-Aminophenyl-β-N-acetylaminopropionic acid (III). 32.4 g of N-acetyl-β-4-nitrophenyl-β-alanine (I) was hydrogenated in 650 ml of alcohol over Raney nickel at 30 atm and 80° until absorption of hydrogen had ceased completely. The alcohol was distilled off in vacuo and the resinous residue was triturated with ether. The product which crystallized out was washed with the same solvent and recrystallized from absolute alcohol. Yield 18.5 g (64.7%). M. p. 146-147° (decomp.). The product (II) is very soluble in water, moderately soluble in alcohol and has poor solubility in acetone; it is insoluble in ether.

Found %: C 59.42, 59.61; H 6.26, 6.31; N 12.14. $C_{11}H_{14}O_3N_2$. Calculated %: C 59.45; H 6.30; N 12.61.

β-(4-Amino-3,5-diiodophenyl)-β-alanine (IV). 18.5 g of the amino acid (II) was refluxed for 2 hours with 185 ml of dilute (1:1) hydrochloric acid. The reaction mixture was diluted with 278 ml of water and 27.4 g of iodine monochloride in 37 ml of dilute (1:1) hydrochloric acid was added dropwise, with stirring, at 35°. After stirring at this temperature for 3 hours, excess iodine was removed by means of sodium bisulfite. The precipitate that separated on standing was filtered off, dissolved in 250 ml of boiling water, the amino acid precipitated with saturated sodium acetate solution and washed with water, alcohol and ether. Yield 16.4 g (44%). M. p. 222-223° (decomp.). The product is soluble in dilute acids and alkalis. It is insoluble in the usual organic solvents.

Found %: I 57.66, 57.50; $H_2O$(Fischer) 4.2. $C_9H_{10}O_2N_2I_2 \cdot H_2O$. Calculated %: I 57.44; $H_2O$ 4.0.

0.3 g of the amino acid (IV) was dissolved in a mixture of 0.5 ml of conc. HCl and 5 ml of water. On standing 0.24 g of β-(4-amino-3,5-diiodophenyl)-β-alanine hydrochloride, characterized by a decomposition temperature of about 183° (with evolution of iodine), separated. This compound is moderately soluble in water and dissolves readily in alcohol.

Found %: Cl (ionic) 7.44, 7.50. $C_9H_{10}O_2N_2I_2 \cdot HCl$. Calculated %: Cl (ionic) 7.57.

β-(3-Aminophenyl)-β-alanine (VI). β-3-Nitrophenyl-β-alanine was prepared by Johnson's modification of the V. M. Rodionov reaction in a medium of n-butyl alcohol. Yield 63%. M. p. 236° (decomp.). 10 g of this amino acid was hydrogenated over Raney nickel (2.5 g) in 173 ml of aqueous alcohol (1:1) at 40 atm and 85-90° until absorption of hydrogen had ceased completely. The catalyst was filtered from the hot solution and the filtrate was evaporated in vacuo to small volume. On cooling a precipitate separated which was recrystallized from aqueous alcohol (1:1). Yield 6 g (63%). M. p. 221-222° (decomp.). Posner [5] gives m. p. 228°.

Found %: C 54.43; H 6.91; N 14.05, 13.97; $H_2O$ (Fischer) 9.20. $C_9H_{12}O_2N_2 \cdot H_2O$. Calculated %: C 54.60; H 6.06; N 14.15; $H_2O$ 9.09.

β-(3-Amino-4,6-diiodophenyl)-β-alanine (VII). A solution of 2.57 g of iodine monochloride in a mixture of 2.2 ml of conc. HCl and 2.2 ml of water was added dropwise with stirring over a period of 30 minutes to a solution of 1.3 g of β-(3-aminophenyl)-β-alanine in a mixture of 0.27 ml of conc. HCl and 22 ml of water at 60°. Heating was continued for a further 2 hours, excess iodine was removed with sodium bisulfite, the solution was treated with activated charcoal and the iodinated amino acid was precipitated by means of saturated sodium acetate solution. The precipitate was washed with water, alcohol and ether and purified by reprecipitation from hydrochloric acid as described above. Yield 1.9 g (61%). M. p. 215-216° (decomp.).

Found %: N 6.40, 6.41; I 58.49, 58.05. $C_9H_{10}O_2N_2I_2$. Calculated %: N 6.24; I 58.79.

For the preparation of the dihydrochloride 1.3 g of this amino acid was dissolved in a mixture of 0.5 ml of conc. HCl and 4 ml of water. The solution was treated with activated charcoal and the dihydrochloride was precipitated by addition of 6.5 ml of conc. HCl. Yield 1.1 g (85%). M. p. 183-184° (decomp.).

Found %: Cl (ionic) 13.68, 13.78. $C_9H_{10}O_2N_2I_2 \cdot 2HCl$. Calculated %: Cl (ionic) 14.06.

β-(3,4,6-Triiodophenyl)-β-alanine (X). A solution of 0.64 g of sodium nitrite in 8.3 ml of water was added dropwise to a solution of 2 g of β-(3-amino-4,6-diiodophenyl)-β-alanine in 10.5 ml of water and 4.55 ml of conc. $H_2SO_4$ at 0-5°. The reaction mixture was stirred at this temperature for 1 hour and then 0.69 g of potassium iodide in 6.3 ml of water was added dropwise to the solution at 0°. After standing at room temperature for 17 hours the mixture obtained was heated to 40° in 5 minutes. Excess iodine was removed with sodium bisulfite and the precipitate was filtered off, washed with water, and dissolved in a mixture of 55 ml of water and 1.5 ml of conc. HCl. The solution was treated with activated charcoal and the amino acid (1.53 g) was precipitated by sodium acetate. After purifying by dissolving in dilute hydrochloric acid, precipitating the hydrochloride with concentrated hydrochloric acid and isolating the free amino acid by means of sodium acetate, β-(3,4,6-triiodophenyl)-β-alanine was obtained with a decomposition temperature of 215° (capillary inserted at 205°, rate of heating 3-4° per minute).

Found %: I 70.21, 70.60. $C_9H_9O_2NI_3$. Calculated %: I 70.11.

Oxidation of β-(3,4,6-triiodophenyl)-β-alanine (X). To a solution of 2 g of (X) in 272 ml of 5% aqueous potassium hydroxide at 40°, 116 ml of a 0.7% solution of potassium permanganate was added dropwise, after which the reaction mixture was heated for a further hour at the same temperature. The temperature was then increased to 75-80° and 230 ml of potassium permanganate solution of the same concentration was added dropwise and heating was continued for 6 hours. Sulfur dioxide was passed through the reaction mixture and the precipitate was filtered off, heated with 25 ml of dilute hydrochloric acid (1:20) and again filtered while still hot. The residue on the filter was stirred and heated with 100 ml of aqueous ammonia (1:2) and filtered, and the filtrate was acidified to Congo with hydrochloric acid. The 2,4,5-triiodobenzoic acid (XI) that precipitated was recrystallized from alcohol. Yield 0.51 g (28%). M. p. 247-248°.

Found %: I 76.61. $C_7H_3O_2I_3$. Calculated %: I 76.20.

No melting point depression was observed on mixing with a sample of 2,4,5-triiodobenzoic acid prepared by the method of Wheeler and Johns [4].

For the preparation of the ethyl ester 1.2 g of our triiodobenzoic acid was dissolved in 62 ml of absolute alcohol containing 0.14 g of potassium hydroxide and the solution was refluxed with 0.2 ml of ethyl iodide for 3.5 hours. M. p. 102-103° (from alcohol).

Found %: I 72.20, 72.68. $C_9H_7O_2I_3$. Calculated %: I 72.15.

A sample of the ethyl ester of the acid synthesized according to Wheeler's method was prepared similarly. The two esters were identical.

## SUMMARY

1. The amino analog of Betazine has been synthesized.

2. It has been established that on iodination of β-(3-aminophenyl)-β-alanine, the triiodo derivative is not formed, but β-(3-amino-4,6-diiodophenyl)-β-alanine, the structure of which has been proved conclusively.

## LITERATURE CITED

[1] V. M. Rodionov, N. N. Suvorov, V. G. Avramenko and L. M. Morozovskaia, J. Gen. Chem. 27, 2234 (1957);*N. N. Suvorov, V. G. Avramenko and L. M. Morozovskaia, Authors' Certificate 104779 (1956).

[2] N. N. Suvorov and A. A. Dudinskaia, J. Gen. Chem. 28, 1371 (1958).*

[3] V. M. Rodionov, N. N. Suvorov and V. G. Avramenko, J. Gen. Chem. 26, 520 (1956).*

[4] H. Wheeler and C. Johns, Am. Chem. J. 44, 441 (1910).

[5] T. Posner, Lieb. Ann. 389, 47 (1912).

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* Original Russian pagination. See C. B. Translation.

# N-OXIDES OF THE QUINOXALINE SERIES

## II. N-OXIDES OF β-(QUINOXALYL-2)-PROPIONIC AND β-(QUINOXALYL-2)-ACRYLIC ACIDS

A. S. Elina

In a previous communication [1] the properties and method of preparation of mono- and di-N-oxides of quinoxalyl-2-carboxylic acid were described; in that work it was shown that the presence of the electrophilic carboxyl group in the position ortho to the nitrogen of the quinoxaline ring hinders its oxidation.* The resistance to oxidation of the nitrogen ($N^1$) in quinoxalyl-carboxylic acid is evidently caused by the displacement of its free electron pair in the direction of the carboxyl oxygen.

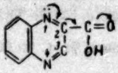
We were interested in the N-oxides of β-(quinoxalyl-2)-propionic acid and its derivatives for the purpose of studying their biological properties.

Since the electrophilic carboxyl group in β-(quinoxalyl-2)-propionic acid is separated from the ring by a two-membered, saturated carbon chain it would be expected that (in contrast to the di-N-oxides of quinoxalyl-2-carboxylic acid) the di-N-oxide of β-(quinoxalyl-2)-propionic acid could be prepared by direct oxidation of the parent acid with hydrogen peroxide.

In fact, β-(quinoxalyl-2)-propionic acid, 1,4-di-N-oxide was obtained in good yield by oxidation of β-(quinoxalyl-2)-propionic acid with 45% $H_2O_2$ in glacial $CH_3COOH$. However, it was shown by carrying out the oxidation under milder conditions (5% $H_2O_2$) that the electrophilic carboxyl group in this case also has some effect on the $N^1$ of the quinoxaline ring because the mono-N-oxide obtained from this reaction proved to be β-(quinoxalyl-2)-propionic acid 4-N-oxide; this effect is evidently an induction effect.

The position of the N-oxide group was proved by reacting the ethyl ester obtained from the β-(quinoxalyl-2)-propionic mono-N-oxide with $POCl_3$ by analogy with the reaction described previously [1, 2]. Since the compound prepared in this way contained organically-combined chlorine and from analytical data it corresponded to ethyl β-(3-chloroquinoxalyl-2)—propionate, it can be concluded that the parent compound is β-(quinoxalyl-2)-propionic acid 4-N-oxide. It is interesting to note that on hydrogenation of β-(quinoxalyl-2)-propionic acid 1,4-di-N-oxide, the oxygen attached to $N^4$ is reduced first. The β-(quinoxalyl-2)-propionic acid mono-N-oxide formed on hydrogenation, which by further reduction gives β-(quinoxalyl-2)-propionic acid, is not identical with β-(quinoxalyl-2)-propionic acid 4-N-oxide.

β-(Quinoxalyl-2)-propionic acid was prepared by hydrogenation of the sodium salt of β-(quinoxalyl-2)-acrylic acid [3]. This acid can be prepared by two methods: either by the method, described in the literature, of reacting 2-methyl quinoxaline with chloral with subsequent alkaline hydrolysis of the reaction product [3], or by condensing 2-quinoxalylaldehyde with malonic acid. In the latter case, if the reaction is carried out in glacial acetic acid, quinoxal-2-malonic acid is obtained and is then decarboxylated by heating in quinoline; if, however, the reaction is carried out in pyridine in the presence of piperidine β-(quinoxalyl-2)-acrylic acid can be obtained directly since the quinoxal-2-malonic acid formed as an intermediate product readily decarboxylates under these conditions.



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* An error was made in communication [1]: the ethyl ester of quinoxalyl-2-carboxylic acid 4-N-oxide has m. p. 116-117°, and not 156-157° as was stated in communication [1].

β-(Quinoxalyl-2)-acrylic acid 1,4-di-N-oxide was prepared by an analogous reaction from 2-quinoxalylaldehyde 1,4-di-N-oxide, the structure of the former being proved by its oxidation with the calculated quantity of $KMnO_4$ in acetone, to the already known quinoxalyl-2-carboxylic acid 1,4-di-N-oxide [1].

I thank Professor O. Iu. Magidson for the interest that he has taken in this work.

## EXPERIMENTAL

β-(Quinoxalyl-2)-acrylic acid 1,4-di-N-oxide. A mixture of 1.9 g of quinoxalyl-2-aldehyde 1,4-di-N-oxide, 1.9 g of malonic acid, 20 ml of dry pyridine and 0.2 ml of piperidine was stirred for 30 minutes at 50° and then at 80° until evolution of $CO_2$ ceased. The reaction mixture was cooled and β-(quinoxalyl-2)-acrylic acid 1,4-di-N-oxide (1.6 g) was filtered off and then purified either by reprecipitation from an $NaHCO_3$ solution or by crystallization from $C_2H_5OH$. A bright-yellow crystalline substance of m. p. 219-220° (decomp.), difficultly soluble in organic solvents, liberates iodine from acidic KI solutions (on heating).

Found %: C 56.96, 56.94; H 3.53, 3.67; N 12.16, 12.07. $C_{11}H_8O_4N_2$. Calculated %: C 56.89; H 3.470; N 12.07.

Oxidation of β-(quinoxalyl-2)-acrylic acid di-N-oxide. 0.1 g of the di-N-oxide in 10 ml of acetone was oxidized with an aqueous solution of 0.18 g of $KMnO_4$ at 20-25°. The $MnO_2$ was filtered off and the filtrate was evaporated down to 1/4 volume in vacuo. On acidification a yellow, crystalline material of m. p. 208-209° (from $CH_3COOH$) separated, that gave a marked melting point depression with the original acid, but gave no depression with quinoxalyl-2-carboxylic acid di-N-oxide [1].

Quinoxalyl-2-malonic acid. A mixture of 5 g of quinoxalyl-2-aldehyde, 5 g of malonic acid and 10 ml of glacial $CH_3COOH$ was stirred for 15 minutes at 63-65°, 0.2 g of activated charcoal was then added and the hot mixture was filtered and allowed to stand for 12 hours at 0°. The quinoxalyl-2-malonic acid that separated, after reprecipitation from $NaHCO_3$ solution was an almost colorless, crystalline material of m. p. 167-168° (decomp.). Yield 3.6 g (46.7%).

Found %: N 11.56, 11.51. $C_{12}H_8O_4N_2$. Calculated %: N 11.47.

β-(Quinoxalyl-2)-acrylic acid. a) Decarboxylation of quinoxalyl-2-malonic acid. A solution of quinoxalyl-2-malonic acid (2 g) in 10 ml of quinoline was heated in a current of $CO_2$ for 1 hour at 164-166°, then cooled and poured into a solution of $NaHCO_3$. The quinoline layer was separated and washed a few times with $NaHCO_3$ solution. β-(Quinoxalyl-2)-acrylic acid was precipitated from the combined alkaline solutions with hydrochloric acid, after treatment with activated charcoal. Yield of unpurified product 1.38 g. M. p. 205-207°.

b) Condensation of quinoxalyl-2-aldehyde with malonic acid in the presence of piperidine. A mixture of 11 g of quinoxalyl-2-aldehyde, 11 g of malonic acid, 50 ml of pyridine and 1.1 ml of piperidine was heated for 1 hour at 70-75° and 1.5 hours at its boiling point, then cooled and poured, with stirring, into an aqueous $NaHCO_3$ solution and extracted a few times with ether. β-(Quinoxalyl-2)-acrylic acid of m. p. 210-212° was isolated from the alkaline solution (after decolorizing with activated charcoal) by means of hydrochloric acid. Yield 11.6 g (83.4%).

Purification of β-(quinoxalyl-2)-acrylic acid. 11.6 g of the impure acid was added to 25 ml of 15% NaOH solution. 50 ml of absolute $C_2H_5OH$ was added to the reaction mixture which was then allowed to stand for 12 hours at 0°. The sodium β-(quinoxalyl-2)-acrylate was filtered off and dissolved in water. Pure β-(quinoxalyl-2)-acrylic acid was isolated from the solution (after decolorizing with activated charcoal) by means of hydrochloric acid. Yield 11.02 g (95%). M. p. 217-218°.

Found %: C 65.86; H 4.19; N 13.98, 13.92. $C_{11}H_8O_2N_2$. Calculated %: C 65.98; H 4.03; N 13.99.

β-(Quinoxalyl-2)-propionic acid 4-N-oxide. A mixture of 2.5 g of β-(quinoxalyl-2)-propionic acid, 50 ml of $CH_3COOH$ and 12 ml of 5% $H_2O_2$ was heated for 20 hours at 50°. The reaction mixture was then evaporated to small volume in vacuo at 40° and ether was added until no further turbidity was caused. β-(Quinoxalyl-2)-propionic acid 4-N-oxide, which is a slightly pink, crystalline material, was filtered off. Yield 1.91 g (75%). M. p. 163-164° (from alcohol).

Found %: N 12.89. $C_{11}H_{10}O_3N_2$. Calculated %: N 12.84.

Ethyl ester of β-(quinoxalyl-2)-propionic acid 4-N-oxide. 2 ml of $H_2SO_4$ (d 1.84) was added gradually to 2.4 g of β-(quinoxalyl-2)-propionic acid 4-N-oxide in 46 ml of absolute $C_2H_5OH$ and the mixture was allowed to stand until all the solid material went into solution (2-3 hours). Part of the alcohol was then distilled off in vacuo and the residue was poured into an $NaHCO_3$ solution containing pieces of ice. The ethyl ester of β-(quinoxalyl-2)-propionic acid 4-N-oxide was extracted with ether. The ethereal solution was dried and the ether distilled off. The residue was crystallized from aqueous $C_2H_5OH$. Pale-yellow needles of m. p. 73-74°. Yield 2.0 g (68.5%).

Found %: C 63.67; H 5.73; N 11.51. $C_{13}H_{14}O_3N_2$. Calculated %: C 63.4; H 5.73; N 11.37.

Ethyl β-(3-chloroquinoxalyl-2)-propionate. 0.50 g of the ethyl ester of β-(quinoxalyl-2)-propionic acid 4-N-oxide was added gradually with cooling to 2.5 ml of $POCl_3$. The solution was then heated at 80-85° for 40 minutes, cooled and poured onto ice, and after standing for an hour it was extracted with ether. After removing the ether 0.42 g of ethyl β-(3-chloroquinoxalyl-2)-propionate remained. A slightly pink, crystalline material of m. p. 78-79° (from aqueous ethanol); insoluble in water, dilute acids and alkalis, soluble in concentrated acid solutions.

Found %: N 10.4; Cl 13.5. $C_{13}H_{13}O_2N_2Cl$. Calculated %: N 10.58; Cl 13.39.

β-(Quinoxalyl-2)-propionic acid 1,4-di-N-oxide. a) A mixture of 83 ml of $CH_3COOH$, 24 ml of 30% perhydrol and 20 ml of acetic anhydride was heated for 3 hours at 50°; 5 g of β-(quinoxalyl-2)-propionic acid was then added and the mixture was kept at 50° for 20 hours. The reaction mixture was evaporated to a small volume in vacuo and 4.15 g (71.5%) of β-(quinoxalyl-2)-propionic acid 1,4 di-N-oxide was isolated by adding ether to the residue. A yellow, crystalline substance of m. p. 184-185° (decomp., from alcohol). Liberates iodine from acidified KI solutions on heating.

Found %: C 56.23; H 4.55; N 12.16, 12.07. $C_{11}H_{10}O_4N_2$. Calculated %: C 56.4; H 4.3; N 11.96.

b) A mixture of 5 ml of $CH_3COOH$, 3 ml of 30% perhydrol and 1.5 ml of acetic anhydride was heated for 3 hours at 40-50°, then 0.3 g of β-(quinoxalyl-2)-propionic acid 4-N-oxide was added and the mixture was maintained at 50° for 20 hours. The reaction mixture was evaporated to a small volume in vacuo, after which ether was added until no more turbidity appeared and 0.2 g of β-(quinoxalyl-2)-propionic acid 1,4-di-N-oxide precipitated, which melted at 184-185° (decomp.) after reprecipitation from $NaHCO_3$ solution, and gave no melting point depression with β-(quinoxalyl-2)-propionic acid 1,4-di-N-oxide prepared by direct oxidation of β-(quinoxalyl-2)-propionic acid.

Reduction of β-(quinoxalyl-2)-propionic acid 1,4-di-N-oxide. 0.5 g of the 1,4-di-N-oxide was dissolved in 12 ml of 8% aqueous NaOH, 0.5 g of moist nickel catalyst was added and the reaction mixture was shaken in a current of hydrogen. Hydrogenation was discontinued when 50 ml of hydrogen had been absorbed. The catalyst was filtered off and β-(quinoxalyl-2)-propionic acid 1-N-oxide (0.30 g) was isolated from the filtrate by addition of hydrochloric acid. A pale-yellow, crystalline material of m. p. 203-204° (decomp., from alcohol).

Found %: C 60.62, 60.79; H 4.65, 4.74; N 12.77. $C_{11}H_{10}O_3N_2$. Calculated %: C 60.54; H 4.62; N 12.84.

0.05 g of β-(quinoxalyl-2)-propionic acid was salted out from the acidified solution by addition of NaCl.

Reduction of β-(quinoxalyl-2)-propionic acid 1-N-oxide. To a solution of 0.15 g of the N-oxide in 4 ml of 2% NaOH solution, 0.1 g of moist nickel catalyst was added and the mixture was shaken in a stream of hydrogen. 15 ml of hydrogen was absorbed. The catalyst was filtered off and β-(quinoxalyl-2)-propionic acid (0.08 g) was precipitated by addition of hydrochloric acid. M. p. 118-119°; a mixed melting point with β-(quinoxalyl-2)-propionic acid prepared in the usual way showed no depression.

## SUMMARY

1. It has been established that on oxidation of β-(quinoxalyl-2)-propionic acid with dilute hydrogen peroxide in acetic acid, a mono-N-oxide is formed, oxidation occurring at the nitrogen in position 4, and when more concentrated hydrogen peroxide solutions are used, oxidation of the second nitrogen also takes place with the formation of β-(quinoxalyl-2)-propionic acid 1,4-di-N-oxide.

2. It has been shown that on hydrogenation of β-(quinoxalyl-2)-propionic acid 1,4-di-N-oxide the $N^4$ oxygen is reduced first, followed by the $N^1$ oxygen.

3. A method of preparation of β-(quinoxalyl-2)-acrylic acid from quinoxalyl-2-aldehyde and malonic acid is proposed.

4. β-(Quinoxalyl-2)-acrylic acid 1,4-di-N-oxide has been prepared by this method from quinoxalyl-2-aldehyde 1,4-N-oxide and malonic acid.

## LITERATURE CITED

[1] A. S. Elina and O. Iu. Magidson, J. Gen. Chem. 25, 161 (1955).*

[2] O. Iu. Magidson and M. V. Rubtsov, J. Gen. Chem. 7, 1896 (1937). S. Meisenheimer, Ber. 59, 1848 (1926); B. Bobransku, L. Kochanska and A. Kowalewska, Ber. 71, 2385 (1938).

[3] R. G. Jones, E. C. Kornfeld and K. C. McLaughlin, J. Am. Chem. Soc. 72, 3539 (1950).

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* Original Russian pagination. See C. B. Translation.

# CARDIAC GLYCOSIDES OF THE SEEDS OF WORM-SEED MUSTARD

## (Erysimum cheiranthoides L.)

N. P. Maksiutina

Worm-seed mustard (Erysimum cheiranthoides L.), is an annual herbaceous plant that grows in all parts of of the European territory of the Soviet Union, in Siberia and in the Far East. The leaves of worm-seed mustard have long been used in popular medicine as a powerful diuretic. A number of authors [1-4) who have studied the infusion and extraction of worm-seed mustard classify it as a plant possessing considerable cardiac activity. Investigators [1-9] studying ultimate preparations of worm-seed mustard observe that these preparations are similar to strophanthin in pharmacological and chemical activity. P. M. Loshkarev [9] in describing the cardiotonically active species of erysimum, regards worm-seed mustard as a valuable medical plant that can serve as an indigenous source for the production of a cardiac preparation very close in properties to strophanthin.

In spite of the considerable interest in this plant, no individual active substance has been isolated up to the present time. The first, preliminary communication of Mushinskii and co-workers [10] on the isolation of three glycosides from the seeds of worm-seed mustard did not appear until 1956. The glycosides were isolated by the method of Reichstein through the products of acetylation and had: first – m. p. 148-150°, second – m. p. 190-195° and third – m. p. 218-221°. All three glycosides did not belong to the main class of physiologically active components since they showed very low biological activity; the activity of the initial chloroform-alcohol extract from which they were prepared was 2-8 times greater.

The object of the present work was to investigate the glycoside composition of the seeds of worm-seed mustard and to isolate the more active glycosides in the crystalline form.

In an investigation of the glycoside composition of the seeds by the method of paper-chromatography, we discovered seven glycosides in more or less significant quantity and three as small traces. We succeeded in isolating two crystalline glycosides of m. p. 196-197° and 224-226° by the method of mild fermentational degradation. The first glycoside named "erysimotoxin" was obtained in a yield of 0.1%; its biological activity in the cat was 0.095 mg/kg body weight*. The second glycoside named "erysin" was obtained in a yield of 0.012%; its biological activity in the cat was 0.11 mg/kg body weight. Both glycosides have high biological activity exceeding in strength the activity of strophanthin, cymarin, digitoxin, convalloside (convallotoxin) and other known cardiac glycosides. The high biological activity and comparatively large yield of erysimotoxin suggest that it is the main active substance of the seeds of worm-seed mustard. According to the physicochemical data obtained, erysimotoxin has one aldehyde group, two secondary and two tertiary hydroxyl groups and an unsaturated, five-membered lactone ring. The aglycon, according to its properties and $R_f$ value, is similar to strophanthidin. The sugar component of erysimotoxin is represented by one molecule of a 2-desoxy sugar. Comparison of the sugar obtained with the known 2-desoxy sugars on paper chromatograms established that it is identical with digitoxose.

On the basis of investigations carried out on the glycoside, its acetyl derivative, the aglycon and the sugar component, the structure given on the next page can be put forward for erysimotoxin.

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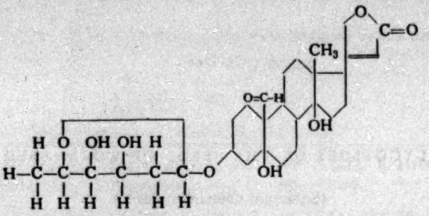
* The biological activity was measured in the pharmacological laboratory of our Institute.



Erysin in chemical respects is also a steroid glycoside with a five-membered lactone ring without a 2-desoxy sugar.

## EXPERIMENTAL

Preparation of erysimotoxin and erysin. 2 kg of seeds was steeped in 2 liters of water and left to stand for two days at room temperature for autolysis. The swollen seeds were ground and the glycosides were extracted from them with a five-fold quantity of water. The seeds were separated in a centrifuge and the aqueous extract was diluted with an equal volume of ethyl alcohol for the precipitation of impurities. The sediment was separated and the filtrate was purified with lead hydroxide [from 1 kg of Pb $(CH_3COO)_2 \cdot 5H_2O$]. The glycosides from the purified filtrate were extracted a few times with chloroform, the extracts evaporated down in vacuo, the residue dissolved in 200 ml of a mixture of chloroform and alcohol (98:2) and the solution chromatographed on aluminum oxide. On elution of the column with a mixture of chloroform and alcohol (98:2) five zones were found, easily visible in UV light. The zones were separated and the glycosides from each zone desorbed separately with ethyl alcohol, the alcohol distilled off and the residues dissolved in alcohol or hot water and left to crystallize. The glycoside erysimotoxin was obtained from the two lower zones in a yield of 0.1%. From the upper zone the other glycoside called erysin was obtained; its yield was 0.012%.

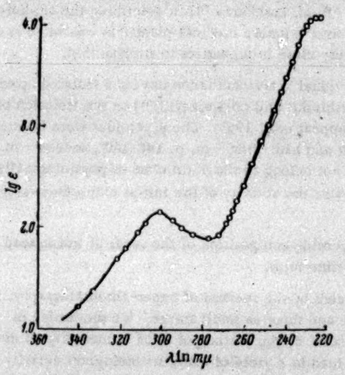


Fig. 1. UV absorption spectrum of erysimotoxin.

Erysimotoxin crystallizes from dilute alcohol in the form of colorless, long plates of m. p. 196-197°. It is readily soluble in dilute alcohol, chloroform, hot water and pyridine, difficultly soluble in cold water and insoluble in ether and petroleum ether. Erysimotoxin gives positive Legal, Liebermann and Keller-Kiliani reactions; in concentrated sulfuric acid it dissolves with a brown coloration, turning to green then to blue.

$[\alpha]^{20}D + 26.77 \pm 2°$ (in alcohol).

For analysis the erysimotoxin was dried in high vacuum for 2 hours at 80°.

Found %: C 63.02; H 8.08. M 551.0. $C_{29}H_{42}O_9 \cdot H_2O$. Calculated %: C 62.97; H 7.96. M 552.63.

The absorption spectrum of erysimotoxin (Fig. 1) has two maxima: $\lambda_{max}$ 302 mμ (log ε 2.17), $\lambda_{max}$ ~ 220 mμ (log ε 4.08).

Erysimotoxin acetate. 0,2 g of erysimotoxin was acetylated with acetic anhydride in pyridine for 48 hours at 30°. After removal of the solvent the acetate crystallized from a mixture of pyridine and water in the form of thick plates of m. p. 232-235°. It is readily soluble in chloroform and alcohol and very difficultly soluble in water. In concentrated sulfuric acid the acetate dissolves with a blue-green coloration, changing to emerald-green then to yellow and blue.

$[\alpha]^{22}_D + 40.6 \pm 2°$ (in chloroform).

The sample was analyzed after drying in high vacuum at 100° for 3 hours.

Found %: C 64.11; H 7.56. M 619.3. $C_{33}H_{46}O_{11}$. Calculated %: C 64.03; H 7.53. M 618.70.

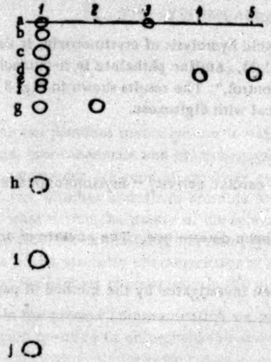


Fig. 2. Positions of the glycoside and aglycon spots on a paper chromatogram: 1) purified extract of worm-seed mustard seeds; 2) erysimotoxin; 3) erysin; 4) erysimotoxigenin; 5) strophanthidin $R_f$ values: a – 0.00, b – 0.03, c – 0.076, d – 0.12, e – 0.15, f – 0.166, g – 0.21, h – 0.40, i – 0.58, j – 0.85.

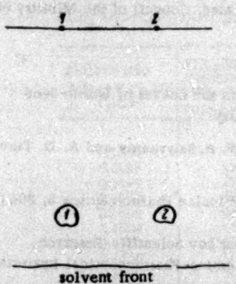


Fig. 3. Position of sugar spots on a paper chromatogram: 1) sugar of m. p. 97-99°; 2) digitoxose ($R_f$ 0.79).

Acid hydrolysis of erysimotoxin. 0.2 g of erysimotoxin was hydrolyzed with 0.3N $H_2SO_4$ solution at room temperature. Hydrolysis took place very rapidly: after only an hour in the acid solution the aglycon began to crystallize in the form of thick plates and nodules. On diluting the acid hydrolyzate with an equal volume of water, the aglycon precipitated out completely. After recrystallizing the aglycon from alcohol, it had m. p. 174-175°, but from a mixture of chloroform and benzene – 232-233°. The aglycon dissolves readily in chloroform and alcohol, with difficulty in benzene and is practically insoluble in water. The aglycon gives positive Legal and Liebermann reactions and a negative Keller-Kiliani reaction. In concentrated sulfuric acid it dissolves with a yellow coloration. It isomerizes in an alkaline medium.

$[\alpha]^{21}_D + 46.3 \pm 2°$ (in alcohol).

Found %: C 68.32; H 7.96. M 404.5. $C_{23}H_{32}O_6$. Calculated %: C 68.29; H 7.97. M 404.

The acidic, aqueous liquor, after separation of the aglycon, was treated twice with 40 ml of a mixture of alcohol and chloroform (1:2), evaporated down a little in vacuo and neutralized with $BaCO_3$. The precipitate was filtered off after thickening with a little kieselguhr and the filtrate was evaporated in vacuo. The residue was dissolved in 5 ml of absolute alcohol, the solution filtered and the alcohol distilled off. The purified syrup was dissolved in a small quantity of dry acetone, diluted with ether and crystallized at 0°. On standing for 46 hours crystals of a sugar of m. p. 97-99° appeared. The crystals gave a positive Keller-Kiliani reaction indicating the presence of a 2-desoxy sugar.

Erysin crystallizes from water in the form of short plates, collected together in clusters, of m. p. 224-226°. It dissolves readily in alcohol and hot water, with difficulty in chloroform and is insoluble in ether. In concentrated sulfuric acid it dissolves with an orange coloration changing to brown and yellow. Erysin gives positive Legal and Liebermann reactions and reduces Fehling's reagent only after acid hydrolysis. The Keller-Kiliani reaction is negative.

Investigation of the glycoside composition of the seeds by the method of paper chromatography. For this investigation an extract from the seeds containing all the glycosides, the glycosides erysimotoxin and erysin, and the aglycons strophanthidin and erysimotoxigenin were taken. Separation was carried out on chromatographic paper (Leningrad factory) in the system formamide-chloroform. The results are shown in Fig. 2, from which it is seen that the purified extract of worm-seed mustard seeds gives ten glycoside spots. Three of these glycosides are present in insignificant quantity ($R_f$ 0.4, 0.58 and 0.85), two have been isolated in crystalline form ($R_f$ 0.00 and 0.21) and the remaining five glycosides ($R_f$ 0.03, 0.076, 0.12, 0.15 and 0.166) have not yet been isolated.

On comparing the aglycon of erysimotoxin (erysimotoxigenin) with strophanthidin, we obtained spots on the chromatogram of almost identical $R_f$ values (0.125 and 0.12). The paper-chromatographic data and other physicochemical properties of the aglycon of erysimotoxin enable the assumption to be made that it is very close to strophanthidin and is possibly identical with it.

For identification of the sugar of m. p. 97-99° obtained from the acid hydrolysis of erysimotoxin, it was chromatographed on paper in the system n-butanol-pyridine-water (3:2:1.5). Aniline phthalate in n-butanol was used to develop the spots. A solution of digitoxose was used as a "control." The results shown in Fig. 3 provide a basis for the conclusion that the sugar obtained by us is identical with digitoxose.

## SUMMARY

1. From the seeds of worm-seed mustard two new glycosides with cardiac activity – erysimotoxin and erysin – have been isolated.

2. The main physicochemical properties of the glycosides have been determined. The acetate of erysimotoxin and the products of acid hydrolysis have been obtained.

3. The glycoside composition of worm-seed mustard seeds has been investigated by the method of paper chromatography. Ten glycosides were discovered in the seeds.

## LITERATURE CITED

[1] M. N. Varlakov, News about Preparations of the All-Union Scientific Research Chemico-Pharmaceutical Institute, No. 7 (1940).

[2] E. Iu. Shass, Phytotherapy, Acad. Med. Sci. USSR Press (1952).*

[3] V. V. Reverdatto, Proc. Acad. Sci. USSR 40, 283 (1943).

[4] S. S. Shestak, Trans. Chkalovsk Med. Inst. No. 11, 88 (1950).

[5] N. V. Vershinin, E. M. Dumenova, L. N. D'iakonova, K. I. Strachitskii and I. L. Zholnov, New Medicinal Plants of Siberia, No. 1, Novosibirsk 65 (1944).

[6] N. V. Vershinin and D. D. Iablokov, Trans. 5th Plenum of the Sci. Med. Council of the Ministry of Public Health RSFSR, Tomsk 125 (1947).

[7] P. I. Bezruk, Pharmacology and Toxicology 5, 43 (1953).

[8] P. I. Bezruk, Pharmacological Study of a Glycoside Preparation from the Leaves of Worm-Seed Mustard – Coresim, Author's Dissertation Summary, Khar'kov (1954)[in Russian].

[9] A. I. Ban'kovskii, F. L. Bumistrov, A. N. Vasina, P. M. Loshkarev, F. A. Satsyperov and A. D. Turova, The Erysimum Series, Moscow 28 (1953)[in Russian].

[10] J. Muszynsky, Z. Jerzmanowska, J. Kaczmarek, J. Superson, Acta Poloniae Pharmaceutica 5, 304 (1956).

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* In Russian.

# INVESTIGATION OF COMPLEX-FORMATION IN SOLUTIONS OF TERNARY SYSTEMS BY PHYSICOCHEMICAL ANALYSIS METHODS

## IX. THE SYSTEMS $AlBr_3$–$(iso\text{-}C_5H_{11})_2O$–$C_6H_5Br$ and $AlBr_3$–$(iso\text{-}C_5H_{11})_2O$–$C_6H_5Cl$

E. Ia. Gorenbein and V. N. Danilova

In our previous investigations it was shown that aluminum bromide with ethyl ether in ethylene bromide, benzene, bromobenzene and chlorobenzene forms two compounds – $AlBr_3 \cdot (C_2H_5)_2O$ and $Al_2Br_6 \cdot (C_2H_5)_2O$ [1-3]. These compounds are good electrolytes even for solvents with a low dielectric constant. It seemed of interest to discover whether aluminum bromide forms molecular compounds of a similar composition with other ethers and to what extent the nature of the solvent affects the complex formation process. In addition to this there was the problem of verifying the rule [4] that if two nonelectrolytes form two or more electrolytes, then examination of the viscosity characteristics as a method of physicochemical analysis will indicate the compound that has the highest conductivity in the given medium.

In the present communication we present the results of investigation of the reaction of isoamyl ether with aluminum bromide in chlorobenzene and bromobenzene as solvents.

### EXPERIMENTAL

Starting materials and method of investigation. Chlorobenzene and bromobenzene were purified as described previously [3]. Aluminum bromide was synthesized from bromine and metallic aluminum [5]; isoamyl ether was prepared according to Gatterman [6]; the carefully purified product was dried initially over fused calcium chloride, then dried and distilled over metallic sodium. The materials obtained were stored in sealed ampoules.

TABLE 1

Viscosity, Density and Electrical Conductivity of the System $AlBr_3$–$(iso\text{-}C_5H_{11})_2O$–$C_6H_5Br$. at 15°.

| Molar ratio $\frac{AlBr_3 + (C_5H_{11})_2O}{C_6H_5Br}$ | $AlBr_3$ in the mixture $AlBr_3 + (C_5H_{11})_2O$ (mole %) | $d_4^{15}$ | $\eta \cdot 10^2$ | $\varkappa \cdot 10^4$ |
|---|---|---|---|---|
| 0.1504 | 0 | 1.3432 | 1.193 | — |
| 0.1495 | 18.92 | 1.4070 | 1.375 | — |
| 0.1495 | 29.38 | 1.4459 | — | 0.36 |
| 0.1498 | 40.44 | 1.4750 | 1.535 | 0.69 |
| 0.1502 | 43.99 | 1.4903 | — | 1.07 |
| 0.1509 | 44.51 | — | — | 1.05 |
| 0.1503 | 48.77 | — | — | 0.78 |
| 0.1496 | 50.11 | 1.5094 | 1.613 | 0.23 |
| 0.1599 | 50.18 | — | — | 0.24 |
| 0.1480 | 54.49 | 1.5260 | 1.647 | 1.39 |
| 0.1483 | 60.20 | 1.5484 | 1.672 | 1.78 |
| 0.1499 | 64.96 | 1.5660 | 1.652 | 1.45 |
| 0.1475 | 72.51 | 1.5819 | 1.642 | — |
| 0.1499 | 75.41 | 1.5894 | — | 0.84 |
| 0.1481 | 78.04 | 1.5982 | 1.638 | 0.77 |
| 0.1510 | 98.55 | 1.6753 | 1.542 | 0.05 |
| 0.1510 | 100 | 1.6623 | 1.520 | — |

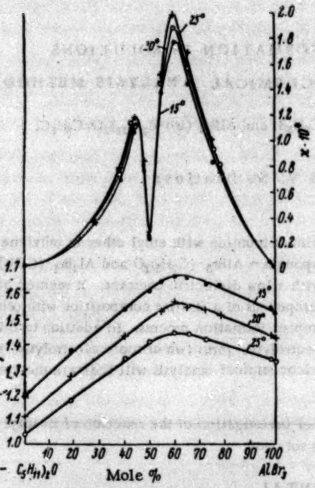


Fig. 1. Variation of viscosity and specific electrical conductivity of the system $AlBr_3$–$(iso\text{-}C_5H_{11})_2O$–$C_6H_5Br$ with ratio of $AlBr_3$ and $(C_5H_{11})_2O$.

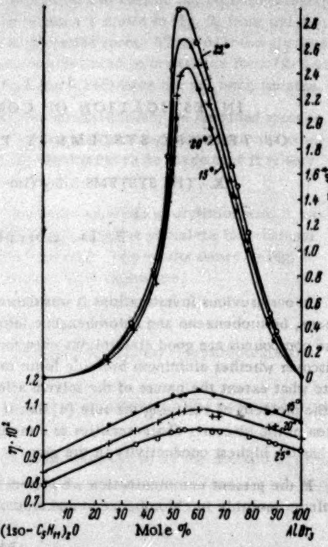


Fig. 2. Variation of viscosity and specific electrical conductivity of the system $AlBr_3$–$(iso\text{-}C_5H_{11})_2O$–$C_6H_5Cl$ with ratio of $AlBr_3$ and $(C_5H_{11})_2O$.

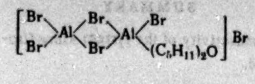
Solutions of isomolar concentration were prepared as described in a previous communication [3].

The viscosity of the solutions was measured with a viscometer [7], and the electrical conductivity and density as described earlier [8, 9]. Investigations were carried out at 15, 20 and 25°.

System $AlBr_3$–$(iso\text{-}C_5H_{11})_2O$–$C_6H_5Br$. Solutions of $AlBr_3$ in bromobenzene are practically nonconducting and according to the results of thermal analysis these components, do not form a compound [10]. On dissolving $AlBr_3$ in $C_6H_5Br$, a slight evolution of heat is observed and the solution becomes red. Addition of isoamyl ether to this solution is accompanied by a marked heat effect. The color of the solution changes from cherry red to light brown. We studied the viscosity, electrical conductivity and density of this system at isomolar concentrations of $AlBr_3 + (iso\text{-}C_5H_{11})_2O$ equal to 0.15 mole per mole of bromobenzene. The results of measurements at 15° are given in Table 1 and the other results are presented graphically.

Figure 1 shows the variation of viscosity and specific electrical conductivity with concentration of the components $AlBr_3 + (iso\text{-}C_5H_{11})_2O$, the mole sum of which is taken as 100%. The viscosity maximum corresponds approximately to the compositions of the compound $Al_2Br_6 \cdot (C_5H_{11})_2O$. The specific electrical conductivity curve has two maxima and a minimum. The first specific electrical conductivity maximum and the minimum correspond to $AlBr_3 \cdot (iso\text{-}C_5H_{11})_2O$. Here, evidently, as in previous cases [2, 3], the formation of a minimum is connected with the conversion of the electrolyte $[AlBr_2 2(C_5H_{11})_2O]\,[AlBr_4]$ to the nonelectrolyte $[AlBr_3(C_5H_{11})_2O]$ according to the scheme $[AlBr_2 2(C_5H_{11})_2O]\,[AlBr_4] \rightleftharpoons 2[AlBr_3(C_5H_{11})_2O]$.

On further increase in concentration of aluminum bromide interaction between $[AlBr_3(C_5H_{11})_2O]$ and $AlBr_3$ takes place with the formation of the compound $Al_2Br_6 \cdot (C_5H_{11})_2O$, which is an electrolyte; its composition can be represented by the formula



This compound corresponds to the second conductivity maximum. It is characteristic that the effect of temperature on electrical conductivity shows up in the region of the electrolyte formed in highest concentration in the solution.

The coincidence of the second conductivity maximum with the viscosity maximum is in full agreement with the above mentioned rule: if two substances form two or more electrolytes, then examination of viscosity characteristics as a method of physicochemical analysis will indicate the compound that has the highest conductivity [4].

TABLE 2

Viscosity, Density and Electrical Conductivity of the System $AlBr_3$–(iso-$C_5H_{11})_2O$–$C_6H_5Cl$ at 15°.

| Molar ratio $\frac{AlBr_3+(C_5H_{11})_2O}{C_6H_5Cl}$ | $AlBr_3$ in the mixture $AlBr_3+(C_5H_{11})_2O$ (mole %) | $d_4^{15}$ | $\eta \cdot 10^2$ | $\varkappa \cdot 10^4$ |
|---|---|---|---|---|
| 0.1500 | 0 | 1.0385 | 0.892 | — |
| 0.1498 | 25.11 | 1.1072 | 1.022 | 0.14 |
| 0.1501 | 35.54 | 1.1388 | 1.059 | 0.39 |
| 0.1493 | 43.92 | 1.1520 | 1.096 | 0.75 |
| 0.1518 | 49.70 | 1.1780 | 1.131 | 1.56 |
| 0.1498 | 52.59 | 1.1883 | 1.133 | 2.06 |
| 0.1467 | 54.18 | 1.1920 | 1.157 | 2.39 |
| 0.1498 | 60.14 | 1.2090 | 1.154 | — |
| 0.1358 | 61.42 | — | — | 2.28 |
| 0.1460 | 65.41 | 1.2230 | 1.142 | 1.96 |
| 0.1496 | 67.70 | 1.2304 | — | — |
| 0.1480 | 73.96 | — | — | 1.45 |
| 0.1491 | 75.73 | — | — | 1.33 |
| 0.1485 | 79.42 | 1.2630 | 1.096 | 1.01 |
| 0.1501 | 87.02 | 1.2855 | 1.072 | 0.44 |
| 0.1499 | 89.32 | 1.2920 | 1.076 | 0.31 |
| 0.1496 | 100 | 1.3234 | 1.028 | — |

$AlBr_3$-(iso-$C_5H_{11})_2O$-$C_6H_5Cl$. No molecular compounds of $AlBr_3$ and chlorobenzene are known. On adding isoamyl ether to a chlorobenzene solution of aluminum bromide, considerable evolution of heat is observed. The color of the solution changes from faint yellow to brown and at ether concentrations greater than 50%, the solution becomes cherry red. Chlorobenzene solutions of $AlBr_3$ and isoamyl ether are more stable than the corresponding bromobenzene solutions

In Table 2 and in Figure 2 results of the investigation of viscosity, electrical conductivity and density of the system $AlBr_3$-(iso-$C_5H_{11})_2O$-$C_6H_5Cl$ at the same isomolar concentrations and temperatures as for the system with $C_6H_5Br$ are given.

The viscosity and specific electrical conductivity curves have a single maximum which evidently indicates the formation of the compound $Al_2Br_6$–$(C_5H_{11})_2O$. Although the left branch of the specific electrical conductivity curve can be regarded as S-shaped, the inflection in which might correspond to the compound $AlBr_3 \cdot (C_5H_{11})_2O$, this inflection is too weakly expressed to enable any conclusion to be drawn. Obviously the difference in the nature of the specific electrical conductivity curves characteristic of the interaction of the same two compounds in the two solvents ($C_6H_5Br$ and $C_6H_5Cl$) must be connected with the nature of the solvents themselves.

It can therefore be considered that $AlBr_3$ and isoamyl ether in bromobenzene as solvent form two complex compounds, and in chlorobenzene only one.

## SUMMARY

1. The viscosity and electrical conductivity of the system $AlBr_3$–(iso-$C_5H_{11}$)$_2$O–$C_6H_5Br$ and $AlBr_3$–(iso-$C_5H_{11}$)$_2$O–$C_6H_5Cl$ at 15, 20 and 25° has been studied.

2. It has been found that under the experimental conditions aluminum bromide and isoamyl ether in bromobenzene forms two compounds $AlBr_3 \cdot (C_5H_{11})_2O$ and $Al_2Br_6 \cdot (C_5H_{11})_2O$, and in chlorobenzene one compound $Al_2Br_6 \cdot (C_5H_{11})_2O$.

3. It is shown that for the section of the system $AlBr_3$–(iso-$C_5H_{11}$)$_2$O–$C_6H_5Br$ studied the rule holds that if two nonelectrolytes interact to form two or more electrolytes, then examination of the viscosity characteristics as a method of physicochemical analysis will indicate which compound in the solution has the highest conductivity.

## LITERATURE CITED

[1] E. Ia. Gorenbein, J. Gen. Chem. 24, 1507 (1954).*

[2] E. Ia. Gorenbein and V. L. Pivnutel', J. Gen. Chem. 27, 20 (1957).*

[3] E. Ia. Gorenbein and V. N. Danilova, J. Gen. Chem. 27, 858 (1957).*

[4] E. Ia. Gorenbein, J. Gen. Chem. 24, 1710 (1954); J. Inorg. Chem. 1, 1877 (1956).

[5] E. Ia. Gorenbein, J. Gen. Chem. 9, 2041 (1939).

[6] L. Gatterman and H. Wieland, Laboratory Methods in Organic Chemistry (Russian translation), State Chem. Press (1948).

[7] A. I. Shatenshtein and Ia. I. Varshavskii, J. Gen. Chem. 22, 1116 (1952).*

[8] E. Ia. Gorenbein, J. Gen. Chem. 23, 1273 (1953).*

[9] E. Ia. Gorenbein, Reports Inst. Chem. Acad. Sci. Ukrainian SSR 1, 213 (1940).

[10] J. J. Burbage and A. B. Garrett, J. Phys. Ch. 56, 730 (1952).

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# THE IRREVERSIBLE-RECIPROCAL SYSTEM FROM SODIUM AND POTASSIUM FORMATES AND THIOCYANATES

N. M. Sokolov and E. I. Pochtakova

A study of reciprocal systems from salts of aliphatic acids and sodium and potassium thiocyanates is undertaken for the purpose of determining the effect of the structure of the aliphatic acid salt radical on the processes in melts of the salts. The binary system NaCNS–KCNS serves as one of the sides of the composition diagram of the systems being studied; the sodium and potassium salts of the homologous series of aliphatic acids, both with straight and branched carbon chains in the radical, are taken as the other salts. In the present work the reciprocal system Na, K ‖ HCOO, CNS is studied.

Sodium thiocyanate does not undergo polymorphic transformations; it is thermally stable up to 500° [1, 2]. Potassium thiocyanate is thermally stable up to 400° [2]; at 142.5° a polymorphic transformation occurs [3]. Sodium formate is stable up to 310° [4]; a polymorphic transformation, as was shown by one of us [5], takes place at 242°. At 370° potassium formate begins to decompose and at 470° decomposition proceeds very rapidly [6]. While investigating the heating of potassium formate with the aid of a differential thermocouple, one of us found that it undergoes polymorphic transformations at 60, 135 and 157° [5].

The heats of formation are known for all the components of the present system: (in kcal/equiv.): NaCNS – 40.36, KCNS – 47.40, HCOONa – 157.7, HCOOK – 160.7 [7]. From these figures it would be expected that the equilibrium in this system would be displaced toward the side of the pair HCOONa and KCNS: $HCOOK + NaCNS \rightarrow HCOONa + KCNS + 4.00$ kcal.

## EXPERIMENTAL

The work was carried out by the visual-polythermic method according to the usual method, a detailed description of which we have given previously [8]. Commercial C.P. or "Pure for Analysis" preparations of the salts were taken for this work and recrystallized – the thiocyanates from alcohol, sodium formate from water and potassium formate from formic acid. The excess acid was removed according to Schlesinger and Martin [9]. The melting points of the components of the system were: sodium thiocyanate 311°, potassium thiocyanate 177°, sodium formate 258° and potassium formate 167°.

### Binary Systems

The system NaCNS-KCNS has a simple eutectic [1]. The branches of the melting-point curve intersect, according to our results, at 126° and 74% KCNS (Fig. 1).

The system HCOONa-HCOOK. Three branches of the melting-point curve intersect in two eutectic points – at 168° and 49.5% HCOOK and at 167° and 96% HCOOK. The composition of the compound formed is 3HCOOK · HCOONa (Fig. 1).

The system KCNS-HCOOK has been investigated by us for the first time. Two branches of the melting point curve intersect in a eutectic point at 83° and 52.5% HCOOK (Fig. 1).

The system NaCNS-HCOONa was first investigated by one of us [8]. Two branches of the melting-point curve intersect in a eutectic point at 189° and 62% HCOONa (Fig. 1).

Numerical data are given in Table 1.

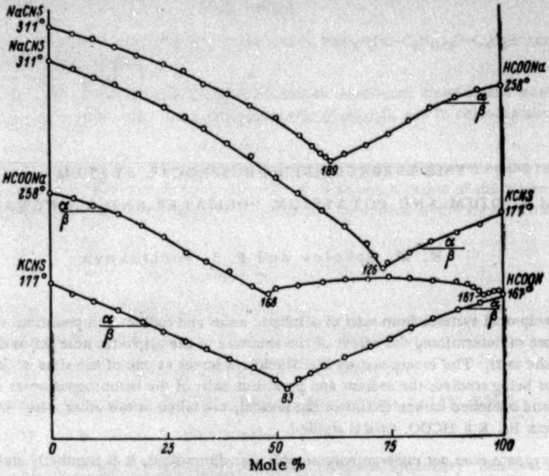

Fig. 1. Melting point diagram of the binary systems.

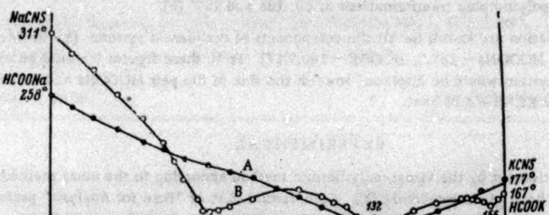

Fig. 2. Diagonal sections of the system: A) stable diagonal section; B) metastable diagonal section.

## TABLE 1

Binary Systems

| NaCNS–KCNS | | HCOONa–HCOOK | | KCNS–HCOOK | | NaCNS–HCOONa | |
|---|---|---|---|---|---|---|---|
| KCNS (moles %) | temp. | HCOOK (moles %) | temp. | HCOOK (moles %) | temp. | HCOONa (moles %) | temp. |
| 0 | 311° | 0 | 258° | 0 | 177° | 0 | 311° |
| 5 | 304 | 5 | 252 | 5 | 168 | 5 | 306 |
| 10 | 298 | 15 | 240 | 10 | 162 | 10 | 298 |
| 15 | 292 | 20 | 232 | 15 | 156 | 15 | 290 |
| 20 | 282 | 35 | 198 | 20 | 145 | 20 | 283 |
| 25 | 272 | 40 | 186 | 25 | 135 | 25 | 278 |
| 30 | 262 | 45 | 176 | 30 | 128 | 30 | 269 |
| 35 | 251 | 47.5 | 170 | 35 | 119 | 35 | 259 |
| 40 | 238 | 49.5 | 168 | 40 | 111 | 40 | 251 |
| 45 | 224 | 52.5 | 173 | 45 | 102 | 45 | 237 |
| 50 | 211 | 55 | 175 | 50 | 91 | 50 | 228 |
| 55 | 195 | 60 | 176 | 52.5 | 83 | 55 | 210 |
| 60 | 178 | 65 | 179 | 55 | 89 | 60 | 195 |
| 65 | 162 | 70 | 180 | 57.5 | 96 | 62 | 189 |
| 70 | 142 | 75 | 182 | 60 | 104 | 65 | 195 |
| 72.5 | 131 | 80 | 181 | 65 | 112 | 70 | 202 |
| 74 | 126 | 85 | 180 | 70 | 119 | 75 | 216 |
| 75 | 127 | 90 | 179 | 75 | 129 | 80 | 225 |
| 80 | 139 | 93 | 177 | 80 | 137 | 85 | 239 |
| 85 | 150 | 94 | 173 | 85 | 147 | 90 | 246 |
| 90 | 158 | 95 | 171 | 90 | 155 | 95 | 256 |
| 95 | 168 | 96 | 167 | 95 | 162 | 100 | 258 |
| 100 | 177 | 97 | 168 | 100 | 167 | | |
| | | 99 | 169 | | | | |
| | | 100 | 167 | | | | |

## TABLE 2

Diagonal sections

| Stable diagonal section HCOONa–KCNS | | Metastable diagonal section NaCNS–HCOOK | | | |
|---|---|---|---|---|---|
| KCNS (moles %) | temp. | HCOOK (moles %) | temp. | HCOOK (moles %) | temp. |
| 0 | 258° | 0 | 311° | 72.5 | 126° |
| 5 | 247 | 5 | 297 | 75 | 139 |
| 10 | 236 | 10 | 281 | 80 | 152 |
| 15 | 227 | 15 | 259 | 85 | 159 |
| 20 | 218 | 20 | 241 | 90 | 165 |
| 25 | 212 | 25 | 215 | 92.5 | 164 |
| 30 | 203 | 27.5 | 201 | 95 | 162 |
| 35 | 194 | 30 | 183 | 96 | 158 |
| 40 | 189 | 32.5 | 163 | 96.4 | 156 |
| 45 | 183 | 34 | 150 | 97 | 158 |
| 50 | 174 | 35 | 151 | 98 | 160 |
| 55 | 166 | 37.5 | 153 | 100 | 167 |
| 60 | 161 | 40 | 156 | | |
| 65 | 147 | 45 | 165 | | |
| 70 | 135 | 50 | 174 | | |
| 71.5 | 132 | 55 | 172 | | |
| 75 | 139 | 60 | 165 | | |
| 80 | 145 | 62.5 | 159 | | |
| 85 | 153 | 65 | 154 | | |
| 90 | 161 | 67.5 | 146 | | |
| 95 | 170 | 70 | 131 | | |
| 100 | 177 | 72 | 124 | | |

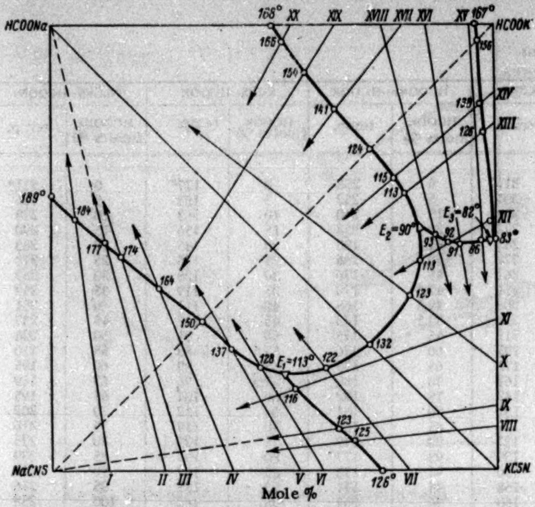
168°
XX
XIX
XVIII
XVII
XVI
XV
167°
HCOONa
HCOOK
166
156
154
141
139
XIV
126
XIII
124
115
113
189°
184
177
174
164
150
137
128
E₁=113°
122
116
132
123
125
113
123
93
E₂=90°
92
91
86
E₃=82°
XII
83°
XI
X
IX
VIII
NaCNS
KCSN
I
II
III
IV
V
VI
126°
VII
Mole %

Fig. 3. Positions of the internal sections in the system Na, K ‖ HCOO, CNS.

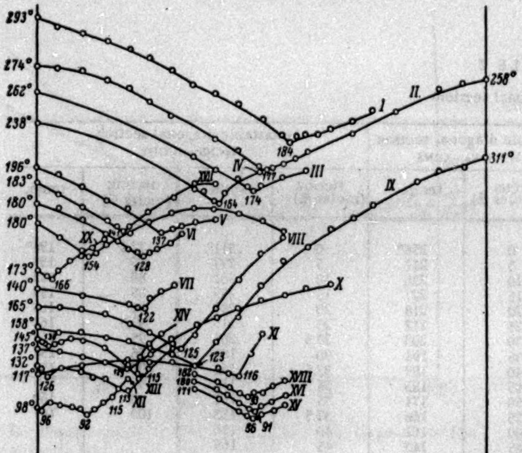

Fig. 4. Internal sections of the irreversible-reciprocal system Na, K ‖ HCOO, CNS.

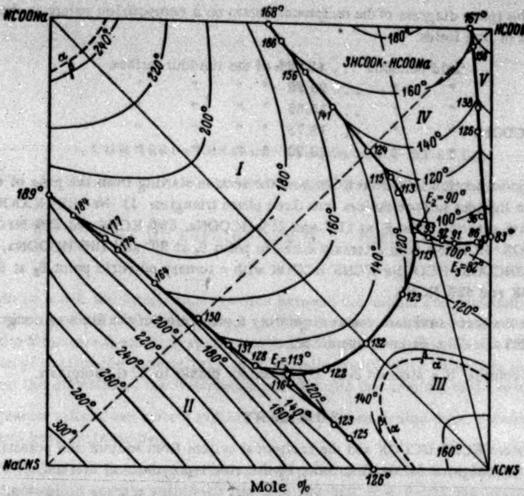

Fig. 5. Projection of the space diagram of the irreversible-reciprocal system Na, K ‖ HCOO, CNS on a composition square.

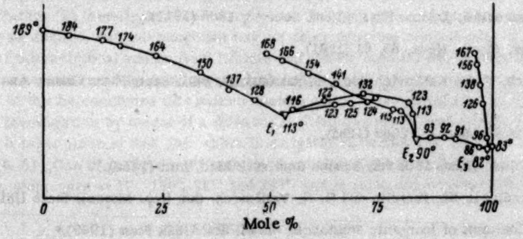

Fig. 6. Projection of lines of congruent crystallization on the NaCNS-KCNS side.

## Diagonal Sections

Two arms of the melting point curve of the stable diagonal cross-section HCOONa-KCNS intersect in a eutectic point at 132° and 71.5% KCNS (Table 2, Fig. 2).

The metastable section NaCNS-HCOOK passes through four fields: 1) NaCNS, 2) HCOONa, 3) 3HCOOK · HCOONa, 4) HCOOK. The four branches of the melting point curve intersect at three points – at 150° and 34% HCOOK, 124° and 72% HCOOK, and 156° and 96.4% HCOOK (Table 2, Fig. 2).

## Internal Section

For demarcation of the crystallization fields of the components and compounds of the system and for locating the three invariant points, 20 sections were drawn. The positions of the sections are shown in Fig. 3. Experimental data relating to the sections are shown in Fig. 4.

## Crystallization Surface of the System

A projection of the space diagram of the reciprocal system on a composition square is shown in Fig. 5. The liquidus surface consists of five fields.

| | | | |
|---|---|---|---|
| The HCOONa | field occupies . . . | 45.82% | of the liquidus surface |
| " NaCNS | " " . . . | 23.98 | " " " " |
| " KCNS | " " . . . | 15.55 | " " " " |
| " 3HCOOK · HCOONa | " " . . . | 13.75 | " " " " |
| " HCOOK | " " . . . | 0.90 | " " " " |

In the stable diagonal section HCOONa—KCNS and the section starting from the pole of the compound 3HCOOK · HCOONa, the liquidus surface divides into three phase triangles: 1) NaCNS—HCOONa—KCNS which corresponds to the ternary eutectic point $E_1$ at 113° and 21% HCOONa, 53% KCNS and 26% NaCNS; 2) HCOONa—KCNS—3HCOOK · HCOONa with a ternary eutectic point $E_2$ at 90° and 16% HCOONa, 45.5% KCNS and 38.5% HCOOK; 3) 3HCOOK · HCOONa—KCNS—HCOOK with a ternary eutectic point $E_3$ at 82° and 0.5% HCOONa, 57.5% HCOOK and 42% KCNS.

In order to define the three invariant points accurately a projection of the lines of congruent crystallization on the NaCNS—KCNS side (Fig. 6) was constructed.

In conclusion we consider it a pleasant duty to express our thanks to A. G. Bergman.

## SUMMARY

1. The binary system KCNS—HCOOK and the reciprocal system from sodium and potassium formates and thiocyanates have been investigated for the first time, by the visual-polythermal method.

2. The tendency of the exchange reaction to move in the direction of the formation of the stable pair of salts HCOONa and KCNS is in agreement with the calculated heat effect of the reaction of 4.00 kcal/equiv.

## LITERATURE CITED

[1] I. B. Vrzhesnevskii, J. Russ. Phys. Chem. Soc. 43, 1368 (1911).

[2] W. B. Gilles, Chem. News. 83, 61 (1901).

[3] M. I. Ravich, V. Ia. Ketkovich and I. S. Rassonskaia, Bull. Sect. Phys. Chem. Analysis, Acad. Sci. USSR 17, 254 (1949).

[4] Merz and Weith, Ber. 15, 2509 (1882).

[5] N. M. Sokolov, Thesis 10th Sci. Session Smolensk Med. Inst. (1956).*

[6] A. A. Balandin, L. Kh. Freidlin and D. N. Vasilevich, Sci. Rep. Moscow State University 6, 321 (1936).

[7] Thermal Constants of Inorganic Substances, Acad. Sci. USSR Press (1949).*

[8] N. M. Sokolov, J. Gen. Chem. 24, 1150 (1954).**

[9] H. J. Schlesinger and A. W. Martin, J. Am. Chem. Soc. 36, 1606 (1914).

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* In Russian.

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# THE IRREVERSIBLE-RECIPROCAL SYSTEM FROM SODIUM AND POTASSIUM ACETATES AND PROPIONATES

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The direction in which the interchange reaction between the sodium and potassium salts of organic acids proceeds in melts has not as yet been investigated. Among the large number of reciprocal systems on which there are data in the literature there is no system consisting of salts of organic acids. The present system is the first link in a chain of systems the general purpose of investigation of which consists in the establishment of the connection between the direction of the interchange reaction and the structure of the salt radicals.

Of the component salts of our system sodium acetate has been studied most, potassium acetate least and the propionates have been little studied.

According to the data in the literature the melting point of sodium acetate lies within the limits of 319-337° [1-7]; that of potassium acetate within the limits of 292-302° [2,4, 8-10], the melting point of sodium propionate was determined by one of us [6] to be 298°; for potassium propionate it was known only that it melts above 300° [11]. All the salts melt without decomposition and are thermally stable up to 390°. Vorlender [12] who noticed a solidification of the salts, discovered the existence of polymorphic transformations in the case of sodium and potassium propionates, but these were not observed in the case of the acetates of these metals. Somewhat later, A. Baskov [2] investigated the binary system from potassium and sodium acetates by the differential-thermal analysis method, but polymorphism was not observed in the original salt. G. G. Diogenov [7] in an investigation of the reciprocal system from lithium and sodium acetates and nitrates obtained a sharp inflection in the sodium acetate melting-point curves, both in the binary systems and within the reciprocal systems, at 323°; on the basis of this he concluded that sodium acetate exists in two modifications, $\alpha$ and $\beta$, at this temperature. However, investigation by means of a differential thermocouple showed that no transformation occurs at this temperature; it takes place at 254° [4]. Other investigators have found no inflections in the sodium acetate curves at 323° [4, 6]. One of us, by the differential-thermal analysis method [13], found polymorphic transformations in sodium propionate at 77°, 195°, 217° and 287°, and in potassium propionate at 330°.

## EXPERIMENTAL

For this work C. P. preparations of the acetates were taken; the propionates were synthesized by a method described earlier [6] starting from the acids and the C. P. carbonates. A commercial preparation of propionic acid was preliminarily purified by redistillation and the propionates obtained were recrystallized from butanol. The melting points of the salts used were: sodium acetate 331°, potassium acetate 301°, sodium propionate 298° and potassium propionate 365°.

The investigation was carried out by the visual-polythermal method in the usual manner. Compositions in the tables are given in molar percentages.

### Binary Systems

1. The system $C_2H_5COONa$–$C_2H_5COOK$ was investigated for the first time. Three branches of the melting point curve intersect in two eutectic points at 288° and 312°, at 8 and 66% potassium propionate. The composition of the compound is $2C_2H_5COONa \cdot 3C_2H_5COOK$.

**TABLE 1**

**Binary Systems**

| $C_2H_5COO \parallel Na, K$ | | $CH_3COO, C_2H_5COO \parallel K$ | | $CH_3COO \parallel Na, K$ | | $CH_3COO, C_2H_5COO \parallel Na$ | |
|---|---|---|---|---|---|---|---|
| $C_2H_5COOK$ (%) | temp. init. crystallization | $C_2H_5COO$ (%) | temp. init. crystallization | $CH_3COOK$ (%) | temp. init. crystallization | $C_2H_5COONa$ (%) | temp. init. crystallization |
| | 298° | 0 | 301° | 0 | 331° | 0 | 331° |
| 5 | 292 | 5 | 310 | 5 | 322 | 5 | 326 |
| 7.5 | 290 | 10 | 311 | 10 | 315 | 10 | 322 |
| 8 | 288 | 15 | 312 | 15 | 307 | 15 | 314 |
| 10 | 294 | 20 | 317 | 20 | 299 | 20 | 311 |
| 15 | 303 | 25 | 320 | 25 | 291 | 25 | 307 |
| 20 | 307 | 30 | 322 | 30 | 282 | 30 | 303 |
| 25 | 310 | 35 | 328 | 35 | 273 | 35 | 301 |
| 30 | 312 | 40 | 331 | 40 | 264 | 40 | 298 |
| 35 | 315 | 45 | 334 | 42.5 | 258 | 45 | 300 |
| 40 | 316 | 50 | 339 | 45 | 254 | 50 | 299 |
| 45 | 317 | 55 | 342 | 47.5 | 247 | 55 | 299 |
| 50 | 317 | 60 | 346 | 50 | 244 | 60 | 298 |
| 55 | 318 | 65 | 348 | 52.5 | 238 | 65 | 297 |
| 60 | 319 | 70 | 352 | 53.5 | 235 | 70 | 296 |
| 66 | 312 | 75 | 356 | 55 | 238 | 75 | 295 |
| 67.5 | 313 | 80 | 358 | 57.5 | 238 | 85 | 294 |
| 70 | 317 | 85 | 362 | 60 | 241 | 90 | 293 |
| 75 | 324 | 90 | 364 | 61.5 | 240 | 95 | 291 |
| 85 | 340 | 95 | 365 | 62.5 | 242 | 97.5 | 295 |
| 90 | 348 | 100 | 365 | 65 | 246 | 100 | 298 |
| 95 | 358 | | | 67.5 | 251 | | |
| 100 | 365 | | | 70 | 255 | | |
| | | | | 75 | 263 | | |
| | | | | 80 | 272 | | |
| | | | | 85 | 282 | | |
| | | | | 90 | 290 | | |
| | | | | 95 | 298 | | |
| | | | | 100 | 301 | | |

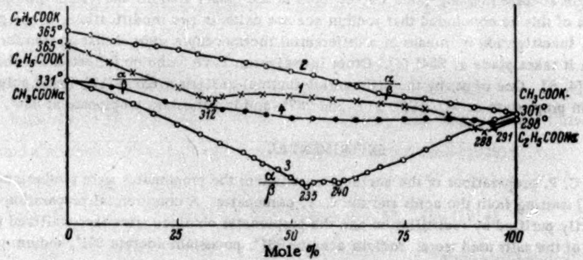


Fig. 1. Melting point diagram of the binary systems: 1) $C_2H_5COOK-C_2H_5COONa$; 2) $C_2H_5COOK-CH_3COOK$; 3) $CH_3COOK-CH_3COONa$; 4) $CH_3COONa-C_2H_5COONa$.

**2. The system $C_2H_5COOK-CH_3COOK$ was investigated for the first time. Here a continuous series of solid solutions occurs with no extremum on the melting point curve.**

**3. The system $CH_3COONa-CH_3COOK$ was first described as a continuous series of solid solutions with a minimum [2], and then as a system with a eutectic [4]. According to our data a compound is formed in this case, of the probable composition – $3CH_3COOK \cdot 2CH_3COONa$. Three branches of the melting point curve intersect in a eutectic point at 235° and 53.5% potassium acetate and in a transition point at 240° and 61.5% potassium acetate.**

**TABLE 2**
**Diagonal Sections**

| $C_2H_5COOK$—$CH_3COONa$ (stable section) | | $C_2H_5COONa$—$CH_3COOK$ (metastable section) | |
|---|---|---|---|
| $CH_3COONa$ (%) | temperature of initial crystallization | $CH_3COOK$ (%) | temperature of initial crystallization |
| 0 | 365° | 0 | 298° |
| 2.5 | 365 | 2.5 | 291 |
| 5 | 364 | 5 | 287 |
| 10 | 353 | 6 | 285 |
| 15 | 344 | 7.5 | 284 |
| 20 | 330 | 10 | 283 |
| 25 | 317 | 15 | 279 |
| 30 | 304 | 17.5 | 273 |
| 35 | 291 | 20 | 272 |
| 40 | 276 | 22.5 | 271 |
| 45 | 260 | 25 | 266 |
| 50 | 247 | 27.5 | 262 |
| 52.5 | 244 | 30 | 257 |
| 55 | 240 | 32.5 | 252 |
| 57 | 236 | 35 | 249 |
| 57.5 | 238 | 36 | 246 |
| 60 | 245 | 37.5 | 245 |
| 65 | 249 | 40 | 243 |
| 75 | 275 | 42.5 | 242 |
| 80 | 287 | 43 | 240 |
| 85 | 296 | 45 | 242 |
| 90 | 308 | 50 | 245 |
| 95 | 321 | 52.5 | 247 |
| 97.5 | 326 | 55 | 248 |
| 100 | 331 | 57.5 | 250 |
| | | 60 | 252 |
| | | 62.5 | 257 |
| | | 65 | 259 |
| | | 67.5 | 262 |
| | | 70 | 264 |
| | | 75 | 269 |
| | | 80 | 278 |
| | | 85 | 285 |
| | | 90 | 289 |
| | | 95 | 293 |
| | | 97.5 | 295 |
| | | 100 | 301 |

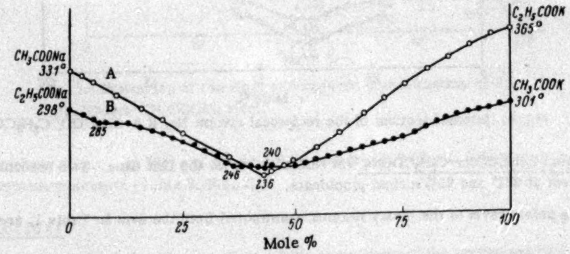
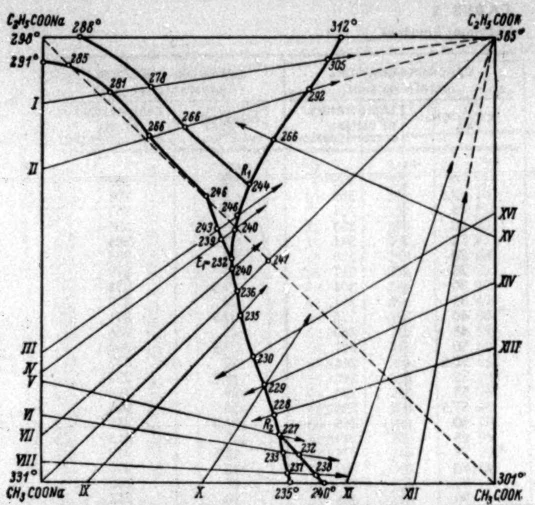


Fig. 2. Diagonal sections of the systems: A) stable diagonal section; B) metastable diagonal section.



C₂H₅COONa
288°
298°
291°
285
281
278
266
266
I
II
R₁
244
246
246
243
240
239
E₁-232
240
241
236
235
230
229
228
R₂
227
232
233
231
238
III
IV
V
VI
VII
VIII
331°
CH₃COONa
IX
X
235°
240°
XI
XII
CH₃COOK
301°
312°
305
292
266
C₂H₅COOK
365°
XVI
XV
XIV
XIII

Fig. 3. Positions of the internal sections of the reciprocal system Na, K ‖ $CH_3COO$, $C_2H_5COO$.

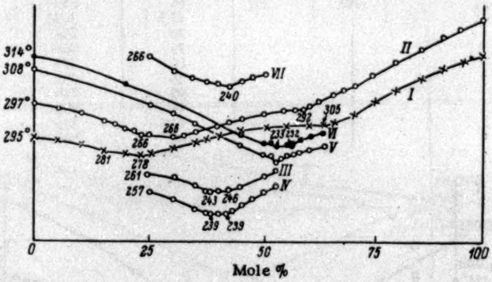


Fig. 4. Internal sections of the reciprocal system Na, K ‖ $CH_3COO$, $C_2H_5COO$.

4. The system $CH_3COONa$–$C_2H_5COONa$ was studied by us for the first time. Two branches of the melting point curve intersect at 291° and 95% sodium propionate.

The melting point curves of the binary systems, constructed from the data in Table 1, are depicted in Fig. 1.

## Diagonal Sections

The stable diagonal section of $C_2H_5COOK$–$CH_3COONa$ has two melting point branches that intersect in a eutectic point at 236° and 57% sodium acetate (Table 2, Fig. 2). The metastable diagonal section of $C_2H_5COONa$–$CH_3COOK$ passes through four fields: twice through the $C_2H_5COONa$ field, the $CH_3COONa$ field and the field of the solid solutions. In conformity with this the melting-point curve consists of four branches

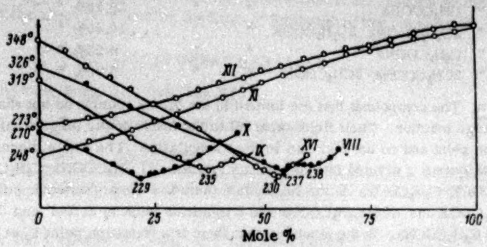


Fig. 5. Internal sections of the reciprocal system Na, K ‖ $CH_3COO$, $C_2H_5COO$.

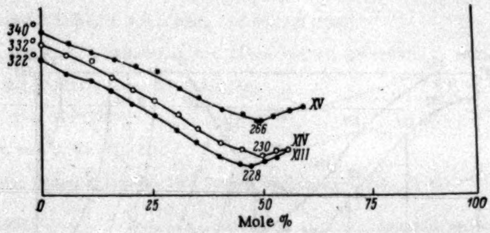


Fig. 6. Internal sections of the reciprocal system Na, K ‖ $CH_3COO$, $C_2H_5COO$.

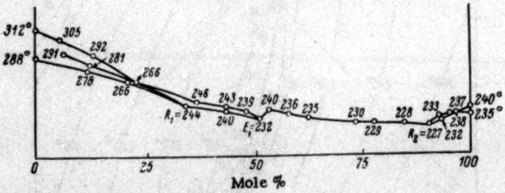


Fig. 7. Projection of the lines of congruent crystallization on the $C_2H_5COONa$–$CH_3COONa$ side.

that intersect in three points: at 285° and 6% potassium acetate, at 246° and 36% potassium acetate and at 240° and 43% potassium acetate (Table 2, Fig. 2).

## Internal Sections

For demarcation of the crystallization fields of the components of the system and of the compounds, and for finding the ternary invariant points, 16 ternary sections were studied, the directions of which are shown in Fig. 3, and the melting point curves of the sections are depicted in Figs. 4-6.

A projection of the lines of congruent crystallization on the $C_2H_5COONa$–$CH_3COONa$ side are given in Fig. 7, and a projection of the space diagram on a composition square is given in Fig. 8.

The liquidus surface of the system consists of five fields:

| | | | |
|---|---|---|---|
| The solid solutions | field occupies . . . | 48.25% | of the liquidus surface |
| " $CH_3COONa$ | " " . . . | 36.20% | " " " " |
| " $2C_2H_5COONa \cdot 3C_2H_5COOK$ | " " . . . | 10.40% | " " " " |
| " $C_2H_5COONa$ | " " . . . | 4.25% | " " " " |
| " $2CH_3COONa \cdot 3CH_3COOK$ | " " . . . | 0.90% | " " " " |

Diagonal system. The compounds that are formed in the binary systems do not show an effect on the direction of the exchange reaction. Their fields taper off to the inside of the diagram of the reciprocal system; they end in a transition point and do not take part in the triangulation. The stable diagonal $C_2H_5COOK$–$CH_3COONa$ system is divided into two ternary systems: 1) $CH_3COONa$–$C_2H_5COONa$–$C_2H_5COOK$ and 2) $CH_3COONa$–$CH_3COOK$–$C_2H_5COOK$. In the first system there is a ternary eutectic point E at 232° and 50.5% $CH_3COONa$, 42% $C_2H_5COOK$ and 7.5% $C_2H_5COONa$ and a transition point $R_1$ at 244° and 33.5% $CH_3COONa$, 45% $C_2H_5COOK$ and 21.5% $C_2H_5COONa$. In the second system there is a transition point $R_2$ at 227° and 11% $C_2H_5COOK$, 47% $CH_3COONa$ and 42% $CH_3COOK$.

We consider it a pleasant duty to thank A. G. Bergman for his valuable advice during the course of this work.

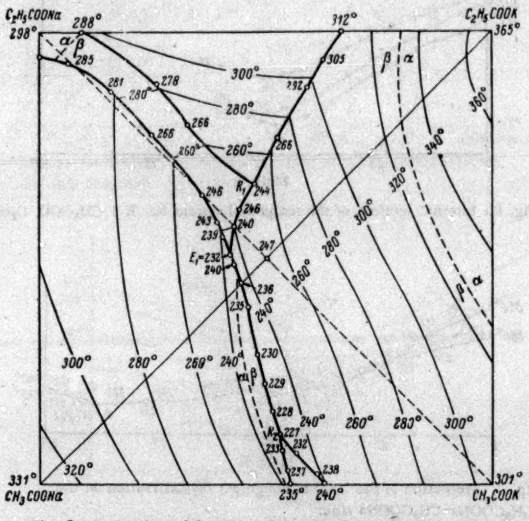

$C_2H_5COONa$
298°
288°
312°
$C_2H_5COOK$
365°
α
β
285
305
β
α
300°
281
280°
278
292
280°
266
266
260°
260°
265
360°
340°
$R_1$
244
246
246
243
240
239
247
$E_1$=232
240
320°
300°
280°
260°
236
235
240°
300°
280°
260°
240°
230
α
β
229
228
240°
260°
280°
300°
β
α
$R_2$
227
233
232
237
238
320°
331°
$CH_3COONa$
235°
240°
301°
$CH_3COOK$

Fig. 8. Projection of the space diagram of the reciprocal system Na, K ∥ $CH_3COO$, $C_2H_5COO$ on a composition square.

## SUMMARY

1. The binary systems $CH_3COO$, $C_2H_5COO$ ∥ K; $CH_3COO$, $C_2H_5COO$ ∥ Na and $C_2H_5COO$ ∥ Na, K have been studied for the first time.

2. Investigation of the binary system from sodium and potassium acetates, in which we established the occurrence of complex formation, has been repeated.

3. The liquidus surface of the irreversible-reciprocal system $CH_3COO$, $C_2H_5COO$ ∥ Na, K has been studied.

4. The equilibrium in the system is displaced towards the side of the higher melting components.

5. It is not possible to check the conformity of the direction of the reaction by mea[illegible] calculated heat effect because of the absence of data on the heats of formation of the propionates.

## LITERATURE CITED

[1] F. G. Schaffgotsch, Pogg. Ann. 102, 295 (1857).

[2] A. Baskov, J. Russ. Phys. Chem. Soc. 47, 1533 (1915).

[3] Green, J. Phys. Chem. 12, 656 (1908).

[4] A. G. Bergman and K. A. Evdokimova, Bull. Sect. Phys.-Chem. Analysis, Acad. Sci. USSR 27, 296 (1956).

[5] N. Sidgwick and J. Gentle, J. Chem. Soc. 121, 1641 (1922).

[6] N. M. Sokolov, J. Gen. Chem. 24, 1581 (1954).*

[7] G. G. Diogenov, J. Inorg. Chem. 1, 799 (1956).

[8] A. Lehrman and E. Leiter, J. Am. Chem. Soc. 60, 142 (1938).

[9] A. Davidson and W. H. McAllister, J. Am. Chem. Soc. 52, 507 (1930).

[10] M. Bakunin and E. Vitali, Gazz. 65, 613 (1935).

[11] Renard, C. r. 104, 916 (1887).

[12] D. Vorlender, Ber. 3, 3120 (1911).

[13] N. M. Sokolov, Theses of Reports, 10th Session Smolensk Med. Inst. (1956).**

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* Original Russian pagination. See C. B. Translation.

** In Russian.

# THE TERNARY SYSTEM FROM LITHIUM AND SODIUM PROPIONATES AND NITRATES

N. M. Tsindrik and N. M. Sokolov

This system is the next link in the chain of systems that are being investigated for the purpose of establishing the relationship between the direction of the exchange reaction between lithium salts of organic acids and sodium nitrate, and the length of the carbon chain in the acid radical.

It was shown earlier that in analogous systems with formates and acetates that the equilibrium is displaced toward the sodium nitrate and lithium fatty-acid-salt side [1, 2]. In the system with acetates the equilibrium is markedly displaced. The present system should provide an answer to the question as to whether the shift increases regularly.

In contrast to the nitrates lithium and sodium propionates have been little studied. Thus, for example, their melting points were first determined by one of us quite recently [4]. Vorlender [5], without stating the temperatures, considered that sodium propionate undergoes polymorphic transformations. One of us found polymorphic transformations for sodium propionate at 77, 195, 217 and 287° [3].

All the salts of the system being studied melt without decomposition. On overheating, the propionates darken and decompose with evolution of gases and in mixtures with nitrates the decomposition is accompanied by ignition.

## EXPERIMENTAL

The system was investigated by the visual-polythermal method according to the generally accepted technique. Commercial preparations of lithium and sodium nitrates were used. C. P. sodium nitrate was purified according to Laiti [6] and "Pure for Analysis" lithium nitrate was twice recrystallized. Lithium and sodium propionates were prepared synthetically by the method described previously [4]. The propionates so obtained were recrystallized from butanol. The initial components of the system had the following melting points; sodium nitrate 308°, lithium nitrate 256°, sodium propionate 298°, lithium propionate 329°.

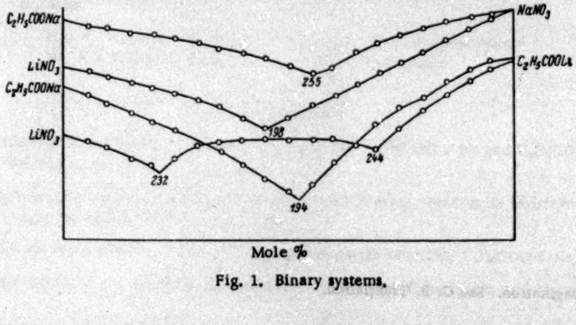

Fig. 1. Binary systems.

## TABLE 1

### Binary Systems

| $LiNO_3$–$NaNO_3$ | | $LiNO_3$–$C_2H_5COOLi$ | | $C_2H_5COOLi$–$C_2H_5COONa$ | | $C_2H_5COONa$–$NaNO_3$ | |
|---|---|---|---|---|---|---|---|
| $NaNO_3$ (mole %) | temp. | $C_2H_5COOLi$ (mole %) | temp. | $C_2H_5COONa$ (mole %) | temp. | $NaNO_3$ (mole %) | temp. |
| 0 | 256° | 0 | 256° | 0 | 329° | 0 | 298° |
| 5 | 250 | 5 | 252 | 5 | 322 | 5 | 294 |
| 10 | 242 | 10 | 246 | 10 | 316 | 10 | 291 |
| 15 | 236 | 15 | 240 | 15 | 304 | 15 | 287 |
| 20 | 230 | 20 | 234 | 20 | 292 | 20 | 284 |
| 25 | 224 | 21.5 | 232 | 25 | 278 | 25 | 282 |
| 30 | 216 | 22.5 | 234 | 30 | 262 | 30 | 280 |
| 35 | 210 | 25 | 238 | 35 | 246 | 35 | 276 |
| 40 | 204 | 30 | 244 | 40 | 226 | 40 | 273 |
| 45 | 198 | 35 | 248 | 42.5 | 218 | 45 | 269 |
| 50 | 208 | 40 | 252 | 45 | 206 | 50 | 264 |
| 55 | 219 | 45 | 253 | 47.5 | 196 | 55 | 258 |
| 60 | 230 | 50 | 252 | 48 | 194 | 60 | 260 |
| 65 | 240 | 55 | 252 | 50 | 198 | 65 | 270 |
| 70 | 250 | 60 | 252 | 52.5 | 204 | 75 | 280 |
| 80 | 270 | 65 | 250 | 55 | 212 | 80 | 286 |
| 90 | 290 | 70 | 244 | 57.5 | 216 | 90 | 298 |
| 100 | 308 | 75 | 266 | 60 | 224 | 95 | 302 |
| | | 80 | 280 | 70 | 248 | 100 | 308 |
| | | 90 | 307 | 80 | 266 | — | — |
| | | 100 | 329 | 90 | 282 | — | — |
| | | | | 100 | 298 | — | — |

## TABLE 2

### Diagonal Sections

| $LiNO_3$–$C_2H_5COONa$ | | | | $C_2H_5COOLi$–$NaNO_3$ | | | |
|---|---|---|---|---|---|---|---|
| $C_2H_5COONa$ (mole %) | temp. | $C_2H_5COONa$ (mole %) | temp. | $NaNO_3$ (mole %) | temp. | $NaNO_3$ (mole %) | temp. |
| 0 | 256° | 37.5 | 260° | 0 | 329° | 60 | 284° |
| 2.5 | 250 | 40 | 270 | 5 | 318 | 70 | 284 |
| 5 | 245 | 42.5 | 280 | 10 | 304 | 80 | 284 |
| 10 | 230 | 45 | 282 | 15 | 286 | 90 | 290 |
| 12.5 | 224 | 50 | 284 | 20 | 270 | 100 | 308 |
| 14.5 | 216 | 55 | 284 | 22 | 264 | | |
| 15 | 218 | 60 | 282 | 25 | 274 | | |
| 17.5 | 224 | 65 | 276 | 30 | 284 | | |
| 20 | 228 | 70 | 260 | 40 | 284 | | |
| 22.5 | 228 | 72.5 | 260 | 50 | 284 | | |
| 25 | 230 | 75 | 240 | | | | |
| 27.5 | 226 | 77.5 | 234 | | | | |
| 29 | 224 | 80 | 244 | | | | |
| 30 | 232 | 85 | 260 | | | | |
| 32.5 | 242 | 90 | 270 | | | | |
| 35 | 252 | 100 | 298 | | | | |

### Binary Systems (Table 1, Fig. 1)

**The system $LiNO_3$–$C_2H_5COOLi$** was investigated for the first time. The melting point curve consists of three branches — the lithium propionate, compound $2C_2H_5COOLi \cdot 3LiNO_3$ and lithium nitrate branches. The branches intersect in eutectic points corresponding to 70 and 22.5% lithium propionate and melting points of 244 and 232° respectively.

The system $C_2H_5COOLi - C_2H_5COONa$. The melting point curve consists of two branches intersecting at 194° and 48% sodium propionate.

The system $C_2H_5COONa - NaNO_3$. The eutectic point corresponds to 56% sodium nitrate and 255° [4].

The system $NaNO_3 - LiNO_3$ recurs in all the ternary reciprocal systems investigated by us from lithium and sodium salts of fatty acids and the nitrates of these metals. The system has a eutectic containing 45% sodium nitrate of m. p. 198°.

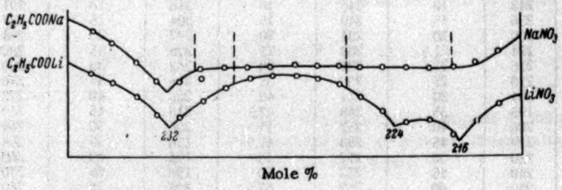

Fig. 2. Diagonal Sections.

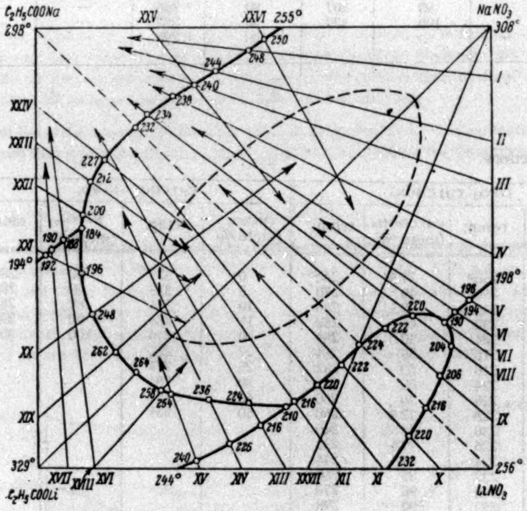
$C_2H_5COONa$
298°
XXV
XXVI 255°
$NaNO_3$
308°
250
248
244
240
238
234
232
227
212
200
184
190
188
192
196
194°
248
262
264
258
254
236
224
210
216
226
240
220
222
224
222
220
190
198
194
204
206
216
220
232
198°
I
II
III
IV
V
VI
VII
VIII
IX
X
XI
XII
XXVII
XIII
XIV
XV
244°
XVI
XVIII
XVII
329°
XIX
XX
XXI
XXII
XXIII
XXIV
256°
$C_2H_5COOLi$
$LiNO_3$

Fig. 3. Positions of the internal sections.

## Diagonal Sections (Table 2, Fig. 2)

The diagonal section $C_2H_5COOLi - NaNO_3$ has a eutectic at 22% sodium nitrate and 264°. On this section stratification was observed from 29 to 85% sodium nitrate.

The diagonal system $LiNO_3 - C_2H_5COONa$ has four primary crystallization branches – the $LiNO_3$, compound $2C_2H_5COOLi \cdot 3LiNO_3$, the interchange product and $C_2H_5COONa$. The inflection points of the branches correspond

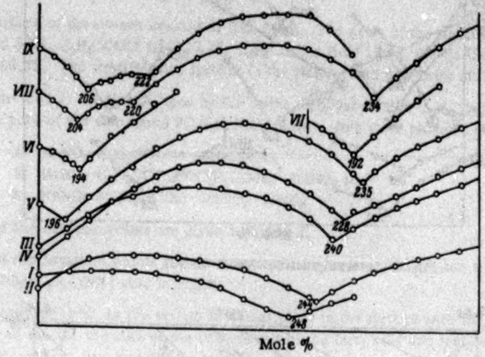

Fig. 4. Internal sections I-IX.

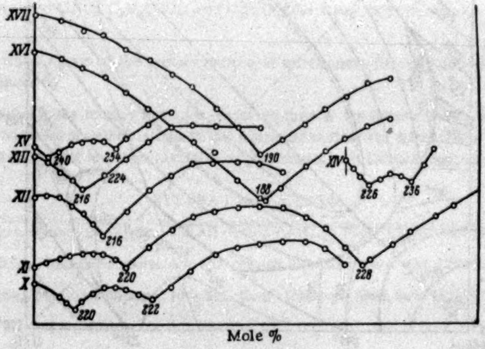

Fig. 5. Internal sections X-XVII.

TABLE 3

| Point | Temperature | Composition of the eutectics (in mole %) | | | |
|---|---|---|---|---|---|
| | | $NaNO_3$ | $LiNO_3$ | $C_2H_5COOLi$ | $C_2H_5COONa$ |
| $E_1$ | 184° | 7.5 | — | 47.5 | 45 |
| $E_2$ | 210 | 14 | 38.5 | 47.5 | — |
| $E_3$ | 190 | 32.5 | 57.5 | 10 | — |

to the coordinates: 14% $C_2H_5COONa$ and 216°, 29% $C_2H_5COONa$ and 224°, 78% $C_2H_5COONa$ and 232°. Stratification was observed in the interval from 38 to 62.5% $C_2H_5COONa$.

For construction of composition diagrams of the ternary system, 27 internal sections of it were investigated, the directions of which are shown in Fig. 3, and the data obtained are presented graphically in Figs. 4-6.

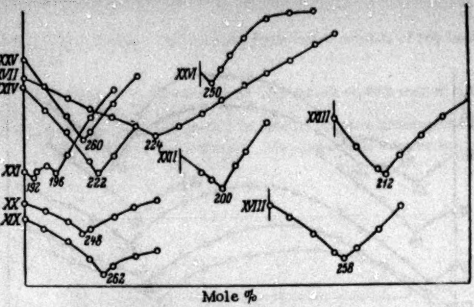

Fig. 6. Internal sections XVIII-XXVII.

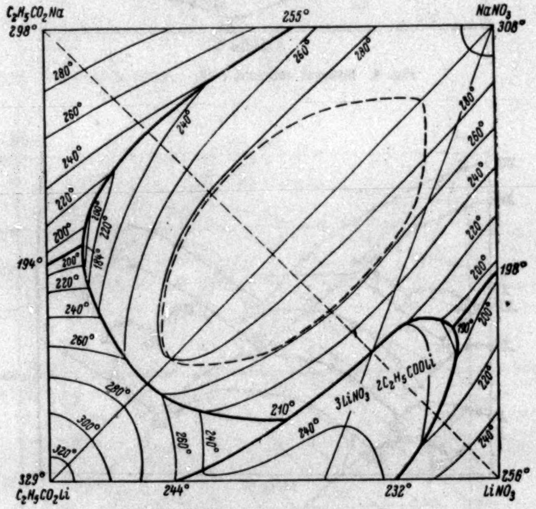
C₂H₅CO₂Na
298°
255°
NaNO₃
308°
280°
260°
240°
220°
200°
194°
200°
220°
240°
260°
280°
300°
320°
329°
C₂H₅CO₂Li
244°
232°
LiNO₃
256°
198°
180°
190°
220°
240°
260°
280°
210°
240°
3LiNO₃
2C₂H₅COOLi

Fig. 7. Ternary reciprocal system.

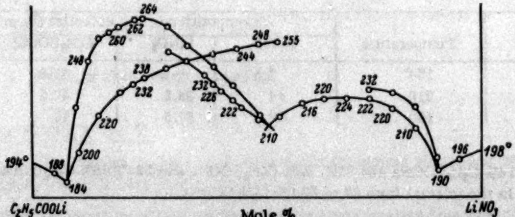

Fig. 8. Projection of invariant points and curves of congruent crystallization of the ternary system Li, Na ‖ $C_2H_5COO$, $NO_3$ on the $LiNO_3$–$C_2H_5COOLi$ side.

Study of the binary systems and the diagonal and internal sections enabled a projection of the space diagram to be constructed on a composition square (Fig. 7).

The liquidus surface of the system consists of five fields. The areas of the fields in percentages of the total are: $LiNO_3$ field 5.07, $C_2H_5COOLi$ field 12.17, $C_2H_5COONa$ field 12.29, the field of the compound 10.74, and the $NaNO_3$ field 59.73. The stratification field is in the $NaNO_3$ field and forms 36.82% of its area.

The system is divided at the $NaNO_3$ apex by the stable diagonal section $C_2H_5COOLi–NaNO_3$ and the section starting from the pole of the compound $2C_2H_5COOLi \cdot 3LiNO_3$, into three phase triangles:

1) $NaNO_3–C_2H_5COONa–C_2H_5COOLi$,
2) $NaNO_3–C_2H_5COOLi–2C_2H_5COOLi \cdot 3LiNO_3$ and
3) $NaNO_3–2C_2H_5COOLi \cdot 3LiNO_3–LiNO_3$.

The positions of the eutectic points are given in Table 3.

The positions of the invariant points and the curves of congruent crystallization are given in the form of projections on the $LiNO_3–C_2H_5COOLi$ side in Fig. 8.

As the results obtained show, in the system investigated as in the systems with formates and acetates, the equilibrium is displaced toward the side of the lithium salt of the fatty acid and sodium nitrate. The nature and extent of the displacement give grounds for considering that there is possibly some regular relationship here. This in its turn involves the question of further investigation in this direction.

## SUMMARY

1. The binary systems $LiNO_3–C_2H_5COOLi$ and $C_2H_5COONa–C_2H_5COOLi$ have been investigated for the first time.

2. A melting point diagram of the ternary reciprocal system from lithium and sodium propionates and nitrates has been obtained.

3. The equilibrium in the ternary system is displaced toward the lithium propionate and sodium nitrate side: with increasing numbers of carbon atoms in the fatty acid radical the displacement of the equilibrium increases in systems consisting of formates, acetates or propionates with lithium and sodium nitrates.

## LITERATURE CITED

[1] N. M. Sokolov, Theses of Reports, 3rd All-Union Conf. on Phys.-Chem. Analysis Moscow (1955).*

[2] N. M. Tsindrik, Theses of Reports, 8th Sci. Session Smolensk Med. Inst. (1956).*

[3] N. M. Sokolov, Theses of Reports, 10th Sci. Conf. Smolensk Med. Inst. (1956).*

[4] N. M. Sokolov, J. Gen. Chem. 24, 1150 (1954).**

[5] D. Vorlender, Ber. 3, 3120 (1911).

[6] Iu. V. Kariakin, Pure Chemical Reagents, State Chem. Press (1947).*

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# COMPLEX COMPOUNDS OF STANNIC CHLORIDE AND BROMIDE WITH UREA

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In a systematic study of the complex compounds of quadrivalent tin with organic compounds containing nitrogen and oxygen we found that thiourea reacts with stannic chloride and bromide with the formation of a complex compound of the composition $SnX_4 \cdot 2(NH_2)_2CS$ [1]. It seemed of interest to us to study the behavior of urea with respect to the quadrivalent tin halides. Taking into consideration the similarity between thiourea and urea we felt that the latter should form compounds of analogous composition with stannic chloride and bromide.

## EXPERIMENTAL

Stannic chloride was purified by multiple redistillation; the fraction boiling at 109° (690 mm) was collected in an ampoule which was then sealed. Stannic bromide was purified in a similar manner. The fraction boiling at 196° (700 mm) was collected in an ampoule; m. p. 29.2°. Acetic acid was fractionally frozen out and then redistilled, the fraction boiling at 113.5° (693 mm) was collected in an ampoule; m. p. 16.57°. Urea was purified by recrystallization from absolute alcohol; m. p. 132.7°.

1. The complex compound of stannic chloride with urea was prepared by direct reaction between stannic chloride and urea in the absence of a solvent. Stannic chloride was mixed with urea in the ratios 1 mole of $SnCl_4$ to 1 mole of $(NH_2)_2CO$ and 1 mole of $SnCl_4$ to 2 moles of $(NH_2)_2CO$. No visible change was observed by the action of stannic chloride on urea at room temperature. However, when the mixture was gently heated, a very vigorous reaction set in and a colorless, crystalline precipitate was formed. On mixing stannic chloride with urea in the ratio 1:1 a precipitate separated and some unreacted stannic chloride remained in the flask. The 1:2 mixture crystallized completely. The solid products obtained were transferred to a glass filter and thoroughly washed with hot benzene. After drying in a vacuum desiccator over $P_2O_5$ they were analyzed for their tin and chlorine contents.

The results of analysis of the product that separated from the 1:2 mixture are given below.

Found %: Sn 31.80, 31.67, 31.89, 31.83; Cl 37.40, 37.31, 37.18, 37.10. $SnCl_4 \cdot 2(NH_2)_2CO$. Calculated %: Sn 31.18; Cl 37.25.

The analysis shows that the tin and chlorine contents of the product are in good agreement with that calculated for a compound of 1:2 composition.

The following results of analysis of the precipitate from the 1:1 mixture were obtained.

Found %: Sn 30.20, 30.29, 30.32, 30.38; Cl 36.42, 36.47. $SnCl_4 \cdot (NH_2)_2CO$. Calculated %: Sn 37.02; Cl 44.23.

The analysis shows that the tin and chlorine content of the product do not correspond to the compound $SnCl_4 \cdot (NH_2)_2CO$ but to the formula $SnCl_4 \cdot 2(NH_2)_2CO$.

The results of analysis of the precipitate formed on addition of stannic chloride to a solution of urea in acetic acid (1 mole of stannic chloride to 4 moles of urea) are given below.

Found %: Sn 30.23, 30.61. $SnCl_4 \cdot 4(NH_2)_2CO$. Calculated %: Sn 23.70.

These figures also indicate that the tin and chlorine contents in the product correspond to the compound $SnCl_4 \cdot 2(NH_2)_2CO$.

It is therefore evident that on mixing stannic chloride with urea in various stoichiometric proportions, only one compound, $SnCl_4 \cdot 2(NH_2)_2CO$, is formed.

We also made a cryoscopic study of the system $SnCl_4$–$2(NH_2)_2CO$ in acetic acid. The variation of the melting point depression with composition, expressed as moles per cent, is shown in Figure 1.

It is seen from the graph that on addition of stannic chloride to a solution of urea in $CH_3COOH$, the magnitude of the depression falls to an equivalent point, then rises a little and finally becomes constant. The constancy of the depression is brought about by the limited solubility of stannic chloride in acetic acid. The equivalent point falls at 33 mole % $SnCl_4$, indicating the formation of a complex compound of stannic chloride and urea of the composition $SnCl_4 \cdot 2(NH_2)_2CO$.

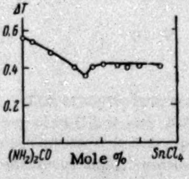

Fig. 1. Cryoscopic titration of a solution of urea in acetic acid with stannic chloride.

2. The complex compound of stannic bromide and urea was prepared by direct interaction of the components in the absence of a solvent. Stannic bromide was mixed with urea in the proportions 1 mole of $SnBr_4$ to 1 mole of $(NH_2)_2CO$ and 1 mole of $SnBr_4$ to 2 moles of $(NH_2)_2CO$. The reaction between stannic bromide and urea was accompanied by considerable evolution of heat. The 1:2 mixture crystallized completely in the form of a yellow material; in the 1:1 mixture, in addition to the compound formed, a certain amount of unreacted stannic bromide remained, which crystallized out at room temperature in the form of colorless, crystalline inclusions.

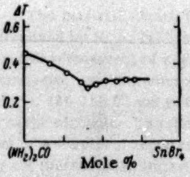

Fig. 2. Cryoscopic titration of a solution of urea in acetic acid with stannic bromide.

The following are the results of analysis of the product obtained from the 1:2 mixture.

Found %: Sn 20.96, 21.00, 21.20; Br 57.51, 57.16, 57.73. $SnBr_4 \cdot 2(NH_2)_2CO$. Calculated %: Sn 21.25; Br 57.23.

From the above figures it is seen that the reaction product from stannic bromide and urea is a compound corresponding to the formula $SnBr_4 \cdot 2(NH_2)_2CO$.

On analysis of the product that separated from the 1:1 mixture the following results were obtained.

Found %: Sn 21.75, 21.54, 21.37, 21.72, 21.36; Br 57.00, 56.66, 56.54, 57.41, 57.39. $SnBr_4 \cdot (NH_2)_2CO$. Calculated %: Sn 23.81; Br 64.13.

The analysis of the precipitate shows that the tin and bromine contents do not correspond to the compound $SnBr_4 \cdot (NH_2)_2CO$, but to the compound $SnBr_4 \cdot 2(NH_2)_2CO$.

The results of a cryoscopic study of the system $SnBr_4$–$(NH_2)_2CO$ in acetic acid are given in Fig. 2 in the form of a graph of melting point depression against composition. On addition of stannic bromide to a solution of urea in $CH_3COOH$ the depression falls to a point of equivalence, then rises a little, after which further addition of stannic bromide does not cause any change in the depression. The constancy of the depression as in the case of stannic chloride, is caused by the limited solubility of stannic bromide in $CH_3COOH$. The inflection point in the curve falls at 33 mole % $SnBr_4$, indicating the formation of the compound $SnBr_4 \cdot 2(NH_2)_2CO$.

Thus, the results of the cryoscopic study of the system $SnBr_4$–$(NH_2)_2CO$, and also the results of analysis of the products, indicate the existence of the compound $SnBr_4 \cdot 2(NH_2)_2CO$.

## SUMMARY

The complex compounds of stannic chloride and bromide with urea, $SnCl_4 \cdot 2(NH_2)_2CO$ and $SnBr_4 \cdot 2(NH_2)_2CO$, have been prepared.

These complex compounds are crystalline substances, stable in air, and have poor solubility in organic solvents.

## LITERATURE CITED

[1] T. N. Sumarokova and E. Sh. Iarmukhamedova, J. Gen. Chem. 26, 3291 (1956).*

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# REDUCTION OF LIMONENE MONOXIDE WITH LITHIUM ALUMINUM HYDRIDE

G. V. Pigulevskii, S. A. Kozhin and V. G. Kostenko

The catalytic hydrogenation of α-oxides of the terpene series to the corresponding alcohols, as was found by one of us [1], is very difficult to achieve. In such cases where this reaction is accomplished under more rigorous conditions, it is accompanied by a number of secondary processes. Thus, on hydrogenation of the oxides of $\Delta^2$-menthene and $\Delta^1$-menthene (carvomenthene) in acetic acid in the presence of hydrated palladium oxide, in addition to the alcohols (the normal products of hydrogenation) p-menthane is obtained and also partial isomerization of the oxides to the ketones takes place; moreover the acetates of the corresponding glycols are also formed. In the case of carvomenthene oxide, the amount of secondary products is as much as 67%. A more convenient method for the conversion of terpene α-oxides to the alcohols is that of reduction of the oxides with lithium aluminum hydride, since this reaction is not usually accompanied by secondary processes.

The material chosen for the present research is limonene monoxide (oxido-1,2-p-menthane-8,9), first synthesized by N. A. Prilezhaev [2]. On reduction of this oxide with lithium aluminum hydride the alcohols, D-neodihydrocarveol of high asymmetric purity ($[\alpha]_D + 32.8°$) and β-terpineol of m. p. 31-31.5°, are formed exclusively. We characterized the two alcohols by means of suitable derivatives: D-neodihydrocarveol hydrate of m. p. 156-156.5° and β-terpineol phenylurethane of m. p. 84-85°. In addition we recorded the Raman spectra of the alcohols. The spectrum of D-neodihydrocarveol is published for the first time. As regards the spectrum of β-terpineol reported in the literature [3], this relates to a mixture of β- and α-terpineol [4]; α-terpineol was not present as an impurity in our sample of β-terpineol.

Our results indicate that the oxide ring of limonene monoxide on reduction opens simultaneously in the two possible directions. On the basis of the magnitude of the optical activity of the mixture of alcohols obtained from the reduction, and also from the ratios of the characteristic spectral lines* in the spectrum of the mixture of alcohols, the conclusion can be drawn that the two alcohols are formed in approximately equal quantities. The results of direct fractionation of the reduction products confirms this view. Excess of reducing agent and further heating of the reaction mixture after mixing of the reagents is complete has practically no effect on the yield of the alcohols.

After our investigation had been completed we became acquainted with the paper of Holub, Herout and Sorm [6], dealing with the synthesis of α-bisabolol. In this work, as one of the intermediate compounds, the reduction product of limonene monoxide with lithium aluminum hydride was used, and the authors considered this to be β-terpineol. The authors of this paper evidently did not take account of the fact that neodihydrocarveol is formed in addition to β-terpineol on reduction of limonene monoxide.

## EXPERIMENTAL

Preparation of limonene monoxide. D-limonene (b. p. 59-60° at 11 mm, $d^{20}_4$ 0.8466, $n^{20}D$ 1.4726, $[\alpha]_D + 126°$), which was used for the preparation of the monoxide, was isolated from caraway oil. Limonene monoxide was synthesized from D-limonene by the action of peracetic acid in ethereal solution [7]. The oxide was characterized by the following constants: b. p. 110-112° at 50 mm, $d^{20}_4$ 0.9324, $n^{20}D$ 1.4671, $[\alpha]_D + 65.5°$.

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* For β-terpineol, as for a tertiary alcohol of the p-menthane series, there is a characteristic line of rocking vibration of the ring with $\Delta\nu$ 721 $cm^{-1}$; for neodihydrocarveol, having a hydroxyl group in the axial position on the secondary carbon atom – a line with $\Delta\nu$ 750 $cm^{-1}$ [5].

**Reduction of limonene monoxide.** 175 ml of an ethereal solution of lithium aluminum hydride (8.1 g of $LiAlH_4$), prepared according to the method of Wieberg and Schmidt [8], was slowly run into 33 g of limonene monoxide dissolved in 275 ml of ether, in a current of dry nitrogen. The reaction mixture was refluxed for 2 hours, then cooled and 100 ml of water was added gradually to the mixture. The main part of the ethereal layer was poured off and the aqueous layer, with the precipitate formed, was treated with 10% aqueous sodium hydroxide solution. The milk-white liquid obtained was extracted with ether. The combined ethereal extracts were dried over potassium carbonate. The reaction product, after removal of the ether, was distilled in vacuo. 27 g (84%) of a mixture of alcohols of b. p. 110-113° at 27 mm, $n^{20}D$ 1.4772, $[\alpha]_D + 18.6°$, was obtained.

Found %: OH 10.70, 10.53. $C_{10}H_{18}O$. Calculated %: OH 11.03.

The reduction of limonene monoxide with lithium aluminum hydride was repeated twice. In one of these experiments the reaction mixture was refluxed for 3 hours; the yield of reduction products was 75%. In the other experiment the reaction mixture, after addition of the $LiAlH_4$ solution, was allowed to stand for only 10 minutes at room temperature before treatment with water; yield 69%.

Separation of the reduction products was carried out by fractionating the mixture in vacuo through a column with an efficiency of 25 theoretical plates. Two main fractions were isolated from the fractionation of 51 g of the mixed reduction products: 1st fraction, b. p. 91-91.5° at 10 mm, 13.8 g (β-terpineol) and 2nd fraction, b. p. 117° at 32 mm, 18.7 g (D-neodihydrocarveol).

### β-Terpineol

B. p. 91-91.5° at 10 mm, m. p. 31-31.5°, $[\alpha]_D$ 0.0°, $d^{20}_4$ 0.9235, $n^{20}D$ 1.4749. Literature data [9]: b. p. 90° at 10 mm, m. p. 32-33°, $d^{20}_4$ 0.9235, $n^{20}D$ 1.4747.

Found %: C 78.21, 78.15; H 11.86, 11.87; OH 11.21. $C_{10}H_{18}O$. Calculated %: C 77.92; H 11.68; OH 11.03.

M. p. phenylurethane 84-85°. Literature data for β-terpineol phenylurethane [9]: m. p. 85°.

### D-Neodihydrocarveol

B. p. 117° at 32 mm, $d^{15}_4$ 0.9337, $n^{20}D$ 1.4798, $[\alpha]_D + 32.8°$. Literature data for L-neodihydrocarveol hydrate [10]: m. p. 214-215°, $d^{15}_4$ 0.930, $n^{20}D$ 1.48016, $[\alpha]_D -32.5°$.

Found %: C 78.12, 77.93; H 11.71, 11.80; OH 10.77. $C_{10}H_{18}O$. Calculated %: C 77.92; H 11.68; OH 11.03.

For the preparation of D-neodihydrocarveol hydrate [11] 4.2 g of D-neodihydrocarveol was shaken for 30 hours with 200 ml of 5% sulfuric acid. The precipitate formed was separated, washed with water and dried. Yield 2.6 g. After two recrystallizations from water, m. p. 156-156.5°, $[\alpha]_D + 40.1°$ (ethanol, C = 10). Literature data for L-neodihydrocarveol hydrate [11]: m. p. 158-159°, $[\alpha]_D -40.0°$.

### Raman Spectra

Spectrum of limonene monoxide. $\Delta\nu$: 240 (3), 289 (5), 323 (3), 393 (3), 502 (2), 526 (2), 556 (1), 612 (2), 674 (9), 693 (2), 757 (8), 794 (3), 841 (6), 883-900 (5), 1041 (3), 1081 (1), 1096 (2), 1119 (2), 1150 (4), 1210 (4), 1303 (5), 1423 (6), 1453 (4), 1643 (10), 2863 (5), 2922 (10), 2983 (5). (Cf. [4]).

Spectrum of the mixture of alcohols obtained on reduction of limonene monoxide. $\Delta\nu$: 278 (1), 303 (1), 340 (1), 395 (2), 444 (2), 502 (3), 539 (2), 605 (1), 723 (6), 752 (7), 797 (1?), 813 (1), 869-894 (5), 915 (1?), 948 (2), 994 (4), 1038 (4), 1076-1118 (5), 1132-1166 (8), 1211 (6), 1220 (6), 1253 (6), 1268 (6), 1434 (8), 1454 (8), 1643 (10), 2868 (4), 2925 (6), 2976 (2).

Spectrum of β-terpineol. $\Delta\nu$: 276 (1), 304 (1), 335 (1), 394 (1), 442 (1), 501 (2), 541 (1), 721 (10), 772 (2), 797 (1), 815 (1), 878 (2), 910 (1), 986-1047 (3), 1135-1169 (7), 1215 (1), 1268 (3), 1395 (1), 1432 (5), 1455 (5), 1642 (8), 2864 (2), 2925 (4), 2970 (2?).

Spectrum of D-neodihydrocarveol. $\Delta\nu$: 302 (1), 391 (1), 439 (1), 501 (1), 561 (1), 715 (1), 750 (10), 801 (1), 859 (1), 882 (2), 942 (2), 990 (2), 1036 (3), 1082 (4), 1101 (4), 1124-1165 (4), 1250 (5), 1309 (4), 1433 (6), 1453 (6), 1641 (8), 2866 (5), 2925 (6).

## SUMMARY

1. It has been established that reduction of limonene monoxide with lithium aluminum hydride takes place with opening of the oxide ring in the two possible directions, with the formation of the tertiary alcohol β-terpineol and the secondary alcohol D-neodihydrocarveol.

2. The Raman spectra of β-terpineol and D-neodihydrocarveol, which has been prepared for the first time, are recorded.

## LITERATURE CITED

[1] G. V. Pigulevskii and S. A. Kozhin, J. Gen. Chem. 27, 803 (1957).*

[2] N. Prileschajew, Ber. 42, 4811 (1909).

[3] G. Bonino and P. Cella, Memorie Reale Accademia Italia 3, Chimica No. 4, 5 (1932).

[4] G. V. Pigulevskii and A. T. Ryskal'chuk, Trans. Komarov BIN, Acad. Sci. USSR Series 5, No. 5, 149 (1955).

[5] G. V. Pigulevskii and S. A. Kozhin, Optics and Spectroscopy, 3, 658 (1957).

[6] M. Holub, V. Herout and F. Sorm, Ceskoslov. farmacie 4, 129 (1955).

[7] B. A. Arbuzov, Research in the Field of Isomeric Transformations of Bicyclic Terpene Hydrocarbons and their Oxides, Kazan 217 (1936).**

[8] E. Wieberg and M. Schmidt in the collection "Lithium" from the series "Rare Metals," Foreign Lit. Press 85 (1954), (Russian translation).

[9] K. Stephan and J. Helle, Ber. 35, 2149 (1902).

[10] H. Schmidt, Ber. 83, 193 (1950).

[11] H. Schmidt, Ber. 88, 453 (1955).

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** In Russian.

## ACADEMY OF SCIENCES USSR PRESS "AKADEMKNIGA" OFFICE

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Transactions of the V. G. Khlopin Radium Institute. Vol. 6. 1957. 167 pp., Price 9 roubles 40 kopecks.

Transactions of the Third All-Union Conference on Colloid Chemistry. (Division of Chemical Sciences of the Academy of Sciences USSR). 1956. 494 pp.. Price 29 roubles.

Figurovskii, N. A. and Iu. I. Solov'ev. Nikolai Nikolaevich Zinin. Biographical Sketch. (Institute of the History of Natural Science and Technique). 1957. 216 pp., 1 insertion. Price 5 roubles.

Chemistry in the Publications of the Academy of Sciences USSR. Vol. 1. No. 2. 1931-1935. Compiled by O. P. Kamenogradskaia and V. P. Alekseeva. 1951. 245 pp. Price 15 roubles 30 kopecks.

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# SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

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|---|---|
| FIAN | Phys. Inst. Acad. Sci. USSR. |
| GDI | Water Power Inst. |
| GITI | State Sci.-Tech. Press |
| GITTL | State Tech. and Theor. Lit. Press |
| GONTI | State United Sci.-Tech. Press |
| Gosenergoizdat | State Power Press |
| Goskhimizdat | State Chem. Press |
| GOST | All-Union State Standard |
| GTTI | State Tech. and Theor. Lit. Press |
| IL | Foreign Lit. Press |
| ISN (Izd. Sov. Nauk) | Soviet Science Press |
| Izd. AN SSSR | Acad. Sci. USSR Press |
| Izd. MGU | Moscow State Univ. Press |
| LEIIZhT | Leningrad Power Inst. of Railroad Engineering |
| LET | Leningrad Elec. Engr. School |
| LETI | Leningrad Electrotechnical Inst. |
| LETIIZhT | Leningrad Electrical Engineering Research Inst. of Railroad Engr. |
| Mashgiz | State Sci.-Tech. Press for Machine Construction Lit. |
| MEP | Ministry of Electrical Industry |
| MES | Ministry of Electrical Power Plants |
| MESEP | Ministry of Electrical Power Plants and the Electrical Industry |
| MGU | Moscow State Univ. |
| MKhTI | Moscow Inst. Chem. Tech. |
| MOPI | Moscow Regional Pedagogical Inst. |
| MSP | Ministry of Industrial Construction |
| NII ZVUKSZAPIOI | Scientific Research Inst. of Sound Recording |
| NIKFI | Sci. Inst. of Modern Motion Picture Photography |
| ONTI | United Sci.-Tech. Press |
| OTI | Division of Technical Information |
| OTN | Div. Tech. Sci. |
| Stroiizdat | Construction Press |
| TOE | Association of Power Engineers |
| TsKTI | Central Research Inst. for Boilers and Turbines |
| TsNIEL | Central Scientific Research Elec. Engr. Lab. |
| TsNIEL-MES | Central Scientific Research Elec. Engr. Lab.–Ministry of Electric Power Plants |
| TsVTI | Central Office of Economic Information |
| UF | Ural Branch |
| VIESKh | All-Union Inst. of Rural Elec. Power Stations |
| VNIIM | All-Union Scientific Research Inst. of Meteorology |
| VNIIZhDT | All-Union Scientific Research Inst. of Railroad Engineering |
| VTI | All-Union Thermotech. Inst. |
| VZEI | All-Union Power Correspondence Inst. |

**Note:** Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. – Publisher.

# DIENE HYDROCARBONS FROM UNSATURATED ALCOHOLS

## II. CATALYTIC DEHYDRATION OF TIGLYL ALCOHOL* AND 2-ETHYLHEXEN-2-OL-1 TO DIENE HYDROCARBONS

Iu. A. Gorin, V. S. Ivanov and E. K. Khrennikova

As we established previously [1], the use of one of the components of Lebedev's catalyst $(B_2)$ and a phosphate catalyst as a dehydrating catalyst makes it possible to prepare divinyl from crotyl alcohol in high yield (up to 88.5%, calculated on the alcohol passed). It appeared interesting to examine the possibility of using these catalysts for the dehydration of other $\alpha,\beta$-unsaturated alcohols in order to obtain from them hydrocarbons with a conjugated system of double bonds. We tested the effect of these catalysts on tiglyl alcohol and 2-ethylhexen-2-ol-1.

D. V. Tishchenko has shown [2,3] that tiglyl alcohol, like the secondary alcohol, isopropenylmethylcarbinol, which is isomeric to it, or a mixture of them, is dehydrated over anhydrous magnesium sulfate at 230-260° to isoprene in a yield of 60% on the alcohol passed and 85-90% on the alcohol reacted. In the present work we show that under the action of one of the dehydration components of Lebedev's catalyst $(B_2)$ and a phosphate catalyst (PH)** [1] tiglyl alcohol may give a yield of isoprene representing 67% of the alcohol passed. Dilution of the starting alcohol vapor with nitrogen did not increase the isoprene yield.

2-Ethylhexen-2-ol-1 may be considered as the intermediate product of the catalytic conversion of n-butyl alcohol to a $C_8$ diene hydrocarbon over Lebedev's catalyst [4]. As the present work established, dehydration of 2-ethylhexen-2-ol-1 gave a mixture of diene hydrocarbons with 8 C-atoms, which contained 2-ethylhexadiene-1,3 and also, possibly, 3-methylheptadiene-3,5. 2-Ethylhexadiene-1,3 was the primary dehydration product. We assume that under the effect of high temperature and the catalyst it was partly isomerized into 3-methylheptadiene-3,5. This hypothesis agrees with the data given by Prevost [5], who showed that dehydration of vinylpropylcarbinol over aluminum oxide at 340°C gave a mixture of hexadiene-1,3 and hexadiene-2,4. The total yields of $C_8H_{14}$ hydrocarbons, prepared by dehydrating the unsaturated alcohol $C_8H_{15}OH$ over the catalysts mentioned above, were 87-95% of the alcohol reacted.

According to I. I. Ostromyslenskii's ideas [6], catalytic dehydration of crotyl alcohol over aluminum oxide proceeds with the intermediate formation of methylallene which then is isomerized to divinyl.

$$CH_3{-}CH{=}CH{-}CH_2OH \xrightarrow{-H_2O} CH_3{-}CH{=}C{=}CH_2 \rightarrow CH_2{=}CH{-}CH{=}CH_2$$

In contrast to Ostromyslenskii, Prevost [7] considers that when dehydrated over aluminum oxide, crotyl alcohol is first isomerized to methylvinylcarbinol which then splits out the elements of water to form divinyl.

$$CH_3{-}CH{=}CH{-}CH_2OH \rightarrow CH_3{-}CHOH{-}CH{=}CH_2 \xrightarrow{-H_2O} CH_2{=}CH{-}CH{=}CH_2$$

Prevost also considers the possibility that water was eliminated from the carbon atoms in the 1,4 positions followed by closing of the bonds.

$$CH_3{-}CH{=}CH{-}CH_2OH \xrightarrow{-H_2O} {-}CH_2{-}CH{=}CH{-}CH_2{-} \rightarrow CH_2{=}CH{-}CH{=}CH_2$$

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* 2-Methylbuten-2-ol-1.

** Used in Germany in the synthetic rubber industry for the dehydration of butylene glycol-1,3 to divinyl [12].

According to the data given by D. V. Tishchenko [2], who obtained isoprene by dehydrating tiglyl alcohol, and according to data from the present work, when dehydrated catalytically, $\alpha,\beta$-unsaturated alcohols of the type $R' - CH_2 - CH = C(R) - CH_2OH$, where R is an alkyl radical and R' hydrogen or an alkyl radical, form hydrocarbons with a conjugated system of double bonds. It follows from this that the reaction cannot proceed through the intermediate stage of the formation of the allene grouping as the $\alpha$-carbon atom lacks the hydrogen required for this. As the elimination of water from crotyl alcohol and from $\alpha,\beta$-unsaturated alcohols which have a substituent alkyl group (methyl or ethyl) in the $\alpha$-position must proceed according to the same mechanism, then Ostromyslenskii's hypothesis cannot be considered as realistic. The problem of whether the allyl rearrangement occurs before dehydration or whether the elements of water are eliminated directly from the 1,4 position, remains unclear and requires further study.

## EXPERIMENTAL

1. Dehydration of tiglyl alcohol. The tiglyl alcohol was obtained by the reduction of tiglaldehyde by the Meerwein-Ponndorf method [8-10]. The tiglaldehyde was obtained by a mixed aldol condensation of acetaldehyde and propionaldehyde in ether in the presence of aqueous alkali [11]. The yield of tiglyl alcohol was 40% of theoretical. The tiglyl alcohol obtained distilled at 135-140° and was characterized by the following constants:

b.p. 135-137°, $d_4^{17}$ 0.8671, $d_4^{20}$ 0.8655, $n_D^{20}$ 1.4420; b.p. 137-140°, $d_4^{17}$ 0.8668, $d_4^{20}$ 0.8653, $n_D^{20}$ 1.4429. According to literature data for tiglyl alcohol: b.p. 136-137°, $d_4^{17}$ 0.8672; b.p. 137-139°, $d_4^{17}$ 0.8667 [2], $n_D^{20}$ 1.4420 [9].

The tiglyl alcohol was dehydrated in the small vertical laboratory furnace, which we described previously [1]. The volume of catalyst was 18 ml. During an experiment, 4-5 ml of alcohol who passed through the furnace. The reaction products were condensed in a condenser and collected in a receiver, cooled with a mixture of ice and salt. Practically no gas formation was observed. Data from the experiments are presented in Table 1.

The isoprene was evaporated off from the condensate in a stream of nitrogen at 60° and passed into a gasometer. The isoprene content of the mixture of nitrogen and isoprene vapor obtained was determined on a sample using maleic anhydride [13]. The gaseous mixture of nitrogen and isoprene was passed through a trap at −60°, into which the isoprene condensed. The portions of isoprene obtained in different experiments were combined and distilled from a flask with a Vigreux distillation column. The distillation yielded a product with b.p. 34.4°, $d_4^{20}$ 0.6808, $n_D^{20}$ 1.4191. According to literature data for isoprene: b.p. 34.5-35°, $d_4^{20}$ 0.6806, $n_D^{20}$ 1.4194 [14]. The adduct obtained from the isoprene and maleic anhydride had m.p. 63°. According to literature data, m.p. 63 – 64° [15].

TABLE 1

Catalytic Dehydration of Tiglyl Alcohol into Isoprene

| Experiment No. | Catalyst | Temperature of experiment | Input rate (ml/hr/ml of catalyst) | Amount of alcohol passed (in g) | Wt. of isoprene obtained (in g) | Yield of isoprene on alcohol passed (in %) |
|---|---|---|---|---|---|---|
| 1 | $B_2$ | 325° | 1.31 | 4.33 | 1.82 | 59.1 |
| 2 | $B_2$ | 325 | 0.56 | 4.33 | 2.08 | 67.6 |
| 3 | $B_2$ | 350 | 0.61 | 4.33 | 1.95 | 63.4 |
| 4 | $B_2$ | 375 | 0.26 | 4.33 | 1.32 | 42.9 |
| 5* | $B_2$ | 350 | 0.63 | 3.46 | 1.64 | 66.8 |
| 6 | Ph | 280 | 0.23 | 3.46 | 1.66 | 67.5 |

* Diluent – nitrogen, degree of dilution – 1 : 3 (mole).

2. Dehydration of 2-ethylhexen-2-ol-1. n-Butyraldehyde was used as the starting material for the preparation of 2-ethylhexen-2-ol-1. It was condensed in the presence of NaOH [16] to give 2-ethylhexen-2-al-1.

The yield of the doubly distilled product was 83%: it had b.p. 168-169°, $d_4^{20}$ 0.8506, $n_D^{20}$ 1.4519. The unsaturated aldehyde obtained was reduced to the corresponding alcohol with aluminum isopropoxide by a procedure similar to that used for the preparation of crotyl and tiglyl alcohols. A second distillation yielded a main fraction with b.p. 179-180° (yield 51.5%), $d_4^{20}$ 0.8568, $n_D^{20}$ 1.45079.

Found %: OH 13.47. Hydrogen number 151. $C_8H_{15}OH$. Calculated %: OH 13.26. Hydrogen number 157.

The α-naphthylurethan was recrystallized from dioxane to give white needles with m.p. 75.5-76.0°.

Found %: N 4.61. $C_{19}H_{23}O_2N$. Calculated %: N 4.71.

The dehydration of 2-ethylhexen-2-ol-1 (see Table 2) was carried out with the apparatus and the catalysts described above. During an experiment 20-50 ml of alcohol was passed.

TABLE 2

Catalytic Dehydration of 2-ethylhexen-2-ol-1

| Expt. No. | Catalyst | Temp. of expt. | Input rate (ml/hr/ml of catalyst) | Am't of alcohol passed (in g) | Wt. of hydrocarbons obtained (g) | Amt. of alcohol reacted (in %) | Yield of $C_8H_{14}$ (in %) on | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | alcohol passed | alcohol reacted |
| 1 | Ph | 280° | 0.33 | 42.90 | 29.78 | 84.8 | 80.7 | 95.1 |
| 2** | Ph | 280 | 0.28 | 17.16 | 7.52 | 60.6 | 51.0 | 89.5 |
| 3 | $B_2$ | 350 | 1.00 | 42.90 | 25.70 | 76.6 | 69.9 | 90.7 |
| 4 | $B_2$ | 350 | 2.10 | 17.16 | 9.65 | 74.1 | 65.4 | 88.2 |

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• Diluent – water, degree of dilution – 1 : 12 (mole).

The hydrocarbons were isolated from the upper layer of the condensate. They were separated from alcohols, either by converting the latter to alcoholates or by converting them to boric esters [17] and then distilling them off from the hydrocarbons.

a) Investigation of hydrocarbons obtained on the phosphate catalyst. 27.87 g of the hydrocarbons was separated into fractions (weight percents are given) by distillation: 1st 120-128°, 10.9%, $n_D^{20}$ 1.4534; 2nd, 128-130°, 3.6%, $n_D^{20}$ 1.4579; 3rd, 130-132°, 13.9%, $n_D^{20}$ 1.4619; 4th, 132-134°, 28.2%, $n_D^{20}$ 1.4667; 5th, 134-135.5°, 28.7%, $n_D^{20}$ 1.4688; residue 12.8%, $n_D^{20}$ 1.4651; losses 1.9%.

The 5th fraction with b.p. 134-135.5° was investigated in detail; it was redistilled over the same range:

$d_4^{20}$ 0.7634, $n_D^{20}$ 1.4694, $MR_D$ 40.23; found 38.21, $EMR_D$ 2.02.
Found %: C 87.03; H 12.82. M 110.4. $C_8H_{14}$. Calculated %: C 87.27; H 12.72. M 110.19.

There is no literature data for 2-ethylhexadiene-1,3; for 3-methylheptadiene-3,5 [18]: b.p. 135.2°, $d_4^{20}$ 0.7652, $n_D^{20}$ 1.4693.

The 5th fraction was hydrogenated in alcohol in the presence of platinum black. The amount of hydrogen added corresponded to 2 moles of hydrogen per mole of diene hydrocarbon. The hydrogenation product was identified as 3-methylheptane:

b.p. 117.5°, $d_4^{20}$ 0.7063, $n_D^{20}$ 1.39885.
Found %: C 84.31; H 16.17. $C_8H_{18}$. Calculated %: C 84.11; H 15.89.

Literature data for 3-methylheptane: b.p. 118.93°, $d_4^{20}$ 0.7058, $n_D^{20}$ 1.3985 [19].

When treated with a saturated $SO_2$ solution, samples of fractions 4 and 5 formed white amorphous precipitates of polymeric sulfone.

Treatment of the 5th fraction with maleic anhydride with heating on a water bath and also at room temperature gave a polymeric product. In toluene at –20°, the reaction led to the formation of a crystalline derivative with m. p. 62° (from ligroin) and a small portion of insoluble (polymeric) product:

Treatment of the 5th fraction with α-naphthoquinone under the conditions described by B. A. Arbuzov and V. S. Abramov [20] led to the formation of an adduct, which appeared as grey scales with m.p. 121° Dehydrogenation of this yielded a tetrahydroanthraquinone derivative – a grey-violet substance, which did not melt at 360°. Oxidation of the latter by Elbs' method [21] gave a finely crystalline substance with a yellow color which did not melt at 350°.

Literature data: for anthraquinonemonocarboxylic acid, m.p. 285-286° [20]; 1,3-anthraquinonedicarboxylic acid does not melt up to 330° [22]; 1,2,4-anthraquinonetricarboxylic acid does not melt up to 320° [23] or decompose at 320° [24].

Found: equiv. 143 (titration in alcohol solution). $C_{14}H_6O_2(COOH)_2$. Calculated: equiv. 148.

The 5th fraction was ozonized in ethyl chloride solution at –70° by the method developed by A. I. Iakubchik [25] for the determination of the vinyl groups in synthetic rubbers. The ozonide was decomposed with hot water and the formic acid in the ozonolysis products determined by the calomel method [26] and the formaldehyde by precipitation with β-naphthol [27]. Found: 63.4% of the hydrocarbon $C_8H_{14}$ had double bonds at the end of the chain (i.e. $>C{=}CH_2$-groups).

The results of ozonization and the data obtained from oxidation of the dehydrogenated condensation product of the hydrocarbon and α-naphthoquinone (formation of anthraquinone dicarboxylic acid) indicates that the fraction contained 2-ethylhexadiene-1,3, $CH_3CH_2CH{=}CH{-}C(C_2H_5){=}CH_2$, with b.p. 134-135.5°, which was the primary dehydration product of 2-ethylhexen-2-ol-1. However, the presence of polymeric product in the adduct, obtained by condensing the hydrocarbon fraction examined with maleic anhydride, and also data on the boiling point, density, refractive index and the ozonization results indicate that the fraction also contained 3-methylheptadiene-3,5. In the literature there is a report [28, 29] that α,α-substituted diene hydrocarbons will condense with maleic anhydride to give polymeric products.

b) Investigation of hydrocarbons obtained on catalyst $B_2$. 25.7 g of the hydrocarbons was distilled to give the following fractions: 1st, 108.5-121.5°, 5.9%, $n_D^{20}$ 1.4369; 2nd, 121.5-129.5°, 24.3%, $n_D^{20}$ 1.4502; 3rd, 129.5-132.5°, 10.7%, $n_D^{20}$ 1.4602; 4th, 132.5-134.0°, 17.2%, $n_D^{20}$ 1.4658; 5th, 134.0-135.5°, 29.6%, $n_D^{20}$ 1.4682; residue 9.8%, $n_D^{20}$ 1.4682; losses 2.3%. The fraction with b.p. 134-135.5° was redistilled over the same range: $d_4^{20}$ 0.7614, $n_D^{20}$ 1.4687.

The combined fractions with b.p. 129.5-135.5° were hydrogenated as described above. The amount of hydrogen added corresponded to 2 moles per mole of $C_8H_{14}$ hydrocarbon. The hydrogenation product isolated was identified as 3-methylheptane:

b.p. 117.8°, $d_4^{20}$ 0.7066, $n_D^{20}$ 1.3982.

Found %: C 83.80; H 15.76. $C_8H_{18}$. Calculated %: C 84.11; H 15.89.

Treatment of samples of fractions 3, 4, and 5 with a saturated solution of $SO_2$ gave white amorphous tablets of a polymeric sulfone. Samples of fractions 1 and 2 gave turbidity but no precipitate.

Treatment of the 5th fraction with maleic anhydride, as described above for experiments on the phosphate catalyst, gave a crystalline product only for condensations in toluene solution at –20° (white needles from ligroin, m.p. 61.5-62°). A mixed melting point with the product obtained from the hydrocarbon in experiments with the phosphate catalyst was not depressed.

Under the same condensation conditions, the hydrocarbon of fraction 4 gave a gelatinous, polymeric mass.

Treatment of the 5th fraction with α-naphthoquinone under the conditions described above, gave a condensation product – dark red needles with m.p. 121.5°. A mixed sample with the analogous product prepared from the hydrocarbon obtained on the phosphate catalyst, melted at 121.0°.

We would like to thank N. G. Kasatkina, who helped us with the ozonization of the hydrocarbon.

## SUMMARY

1. The catalytic dehydration of tiglyl alcohol to isoprene on one of the dehydrating components of Lebedev's catalyst ($B_2$) and a phosphate catalyst, used for the industrial production of divinyl from butylene glycol-1,3 was investigated. The yield of isoprene on the above catalysts represented 67% of the tiglyl alcohol passed.

2. Catalytic dehydration of 2-ethylhexen-2-ol-1 over the same catalysts was investigated. The hydrocarbon yield (calculating on $C_8H_{14}$) was 80% of alcohol passed and 95% of that reacted over the phosphate catalyst and 70% of alcohol passed and 90% of that reacted over catalyst $B_2$. It was shown that the $C_8H_{14}$ hydrocarbons prepared on the two catalysts were identical and that they consisted mainly of 2-ethylhexadiene-1,3, which was the primary dehydration product.

3. As the catalytic dehydration of crotyl alcohol and of α,β-unsaturated alcohols, with an alkyl group in the α-position, to form conjugated dienes probably proceed by the same mechanism. Ostromyslenskii's hypothesis that a compound with an allene grouping may be formed as an intermediate stage should be considered groundless.

## LITERATURE CITED

[1] Iu. A. Gorin, V. S. Ivanov, E. S. Bogdanova, and E. A. Piaivinen, J. Gen. Chem., 28, 169 (1958).*

[2] D. V. Tishchenko, J. Gen. Chem., 6, 1549 (1936).

[3] D. V. Tishchenko, Authors Cert. 46571, April 30, 1936.

[4] Iu. A. Gorin, and F. A. Vasil'eva, J. Gen. Chem., 17, 693 (1947).

[5] Ch. Prevost, C. r., 182, 853 (1926).

[6] I. I. Ostromyslenskii, J. Russ. Chem. Soc., 47, 1472 (1915).

[7] Ch. Prevost, Ann. Chim., [10], 10, 113 (1928).

[8] Org. Reactions, Coll. 2, 194 (1950).**

[9] W. Oroshnik and R. A. Mallory, J. Am. Chem. Soc. 72, 4608 (1950).

[10] A. Lauchbenauer and H. Schinz, Helv. Chim. Acta, 34, 1514 (1951).

[11] V. Grignard and P. Abelmann, Bull. Soc. Chim. (IV), 7, 638 (1949).

[12] J. W. Reppe. Acetylene Chemistry, N. Y., 10 (1949).

[13] A. I. Guliaeva, V. F. Polikarpova, and Z. K. Remiz, Analysis of the Products of Divinyl Production from Ethyl Alcohol by S. V. Lebedev's Method, State Chem. Inst., 60 (1950).

[14] Dict. of Org. Cmpds., Foreign Lit. Press, 2, 448 (1949) [Russian translation].

[15] J. Boeseken, W. J. F. de Rijck van der Gracht, Rec. trav. chim., 56, 1203 (1937).

[16] V. S. Batalin and S. E. Slavina, J Gen. Chem., 7, 202 (1937).

[17] S. M. Rivkin, Caoutchouc and Rubber, No. 3, 16 (1937).

[18] A. L. Henne and A. Turk, J. Am. Chem. Soc, 64, 826 (1942).

[19] M. P. Doss, Physical Constants of Principal Hydrocarbons 2, N.Y. (1943).

[20] B. A Arbuzov and V. S. Abramov, J. Gen. Chem. 57, 977 (1935).

[21] K. Elbs, J. Pr. Ch., 41, 21 (1890).

[22] Beilst., X, 918, (1927).

[23] Beilst., X, 935 (1927).

[24] L. F. Fieser and E. L. Martin, J. Am. Chem. Soc., 58, 1443 (1936).

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*See C.B. Translation.

**In Russian.

[25] A. I. Iakubchik, A. A. Vasil'ev, and V. M. Zhabina, J. Appl. Chem., 17, 107 (1944).

[26] H. Fincke, Bioch. Z., 51, 253 (1913).

[27] K. Fosse, P. Gralve, and P. Thomas, C. r., 200, 1450 (1935).

[28] E. H. Farmer and F. L. Warren, J. Chem. Soc., 1931, 3221.

[29] G. R. Bacon and E. H. Farmer, J. Chem. Soc., 1937, 1065.

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# INVESTIGATION OF CONJUGATED SYSTEMS

## LXXXVII.* ADDITION OF α-CHLORO- AND α-BROMO-ETHERS TO CHLOROPRENE

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The addition of halogen derivatives to diene compounds has been studied on very few examples [1]. The order of addition of α-chloro-ethers to divinyl has been investigated quite thoroughly [2, 3]. B. A. Arbuzov and A. N. Pudovik estiblished that in the case of divinyl, mostly 1,2-products are formed; however, the addition catalyst ($ZnCl_2$) induced isomerization of the latter to 1,4-products, which predominate in the final reaction mixture. The yield of alkoxychloroisohexenes was low (30-37%) on reacting α-chloro-ethers with isoprene (mainly 1, 4-addition) [4]. The decrease in the yield of the primary addition products (in a ratio of 1 : 1) is due to the fact that in the case of isoprene these products have a stronger tendency for telomerization than in the case of divinyl [5].

There are also data on the order of addition of alkyl halides to divinyl and isoprene and of polyhalomethanes and ethanes to divinyl [1, 5]. The addition of α-halo-ethers to diene halogen derivatives has not been studied.

We decided to establish the order of addition of α-chloro- and α-bromo-ethers to chloroprene. As a result of reacting chloroprene with α-halo-ethers one might expect the formation of the following six isomers:

$CH_2Cl-CCl(CH_2OR)-CH=CH_2$ (I), $CH_2=CCl-CHCl-CH_2-CH_2OR$ (IV),
$CH_2OR-CH_2-CCl_2-CH=CH_2$ (II), $CH_2Cl-CCl=CH-CH_2-CH_2OR$ (V),
$CH_2=CCl-CH(CH_2OR)-CH_2Cl$ (III), $CH_2OR-CH_2-CCl=CH-CH_2Cl$ (VI).

The substances actually obtained boiled over a narrow temperature range. Their constants are given in Table 1.

TABLE 1

| $CH_2OR-CH_2-CCl=CH-CH_2Hlg$ | | Boiling point (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ | | Hlg (%) | | Yield (in %) |
|---|---|---|---|---|---|---|---|---|---|
| R | Hlg | | | | found | calc. | found | calc. | |
| $CH_3$ | Cl | 48.9—49.1° (2)<br>79.5—81 (10) | 1.1613 | 1.4770 | 41.05 | 40.82 | 41.48 | 41.95 | 53 |
| $C_2H_5$ | Cl | 55.8—56° (2)<br>86.6—87.4 (10) | 1.1156 | 1.4724 | 45.94 | 45.44 | 38.11 | 38.73 | 67 |
| $C_3H_7$ | Cl | 68.9—69.1 (2) | 1.0901 | 1.4700 | 50.40 | 50.05 | 36.21 | 35.98 | 63 |
| $C_3H_7$-iso | Cl | 60.2—60.3 (2) | 1.0831 | 1.4660 | 50.45 | 50.05 | 35.75 | 35.98 | 64 |
| $CH_3$ | Br | 72.5—73 (5) | 1.4297 | 1.5070 | 44.44 | 43.72 | 54.33 | 54.04 | 70 |
| $C_2H_5$ | Br | 85.3—86.1 (5) | 1.3539 | 1.4998 | 49.41 | 48.33 | 51.06 | 50.76 | 78 |
| $C_3H_7$ | Br | 76.5—77.5 (2) | 1.3075 | 1.4922 | 53.61 | 52.95 | 47.64 | 47.77 | 49 |
| $C_3H_7$-iso | Br | 68 —68.2 (2) | 1.2984 | 1.4900 | 53.78 | 52.95 | 48.18 | 47.77 | 50 |

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* Diene compounds, LXVI. Reactions of dienes with halogen derivatives. III.

The data in Table 1 show that over the series of chloro- and bromo-ethers there is a regularity in the increase in boiling points and the decrease in specific gravities and refractive indexes. A molecular refraction greater than that calculated was found for all the ethers, with a difference of 0.4 in the chloro-ether series and 0.7-1 in the bromo-ether series. This phenomenon has been observed several times in the case of materials with similar structures.

TABLE 2

| Substance | Boiling point (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ |  | Found (%) |  |  |  |  | Calculated (%) |  |  |  |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  | found | calc. | C | H | Cl | N | OR | C | H | Cl | N | OR |
| $CH_3OCH_2-CH_2-CCl=CH-CH_2OCH_3$ | 53.5—53.6° ( 2)<br>77 —78.6 (10) | 1.0622 | 1.4572 | 42.23 | 42.21 | 46.96,<br>49.61 | 8.04,<br>7.65 | —<br>— | —<br>— | 37.80,<br>37.20 | 51.07 | 7.96 | 21.54 | — | 37.70 |
| $C_2H_5OCH_2-CH_2-CCl=CH-CH_2OC_2H_5$ | 66.5—67 ( 2)<br>92 —94 (10) | 1.0239 | 1.4552 | 51.08 | 51.45 | 55.31,<br>54.40 | 8.89,<br>8.88 | 18.63,<br>18.79 | —<br>— | 45.95,<br>46.80 | 56.10 | 8.89 | 18.41 | — | 46.77 |
| $CH_3OCH_2-CH_2-CCl=CH-CH_2N(C_2H_5)_2$ | 88.5—89 ( 5)<br>102 —103.5 (10) | 0.9684 | 1.4610 | 58.30 | 58.03 | 59.64,<br>59.36 | 9.69,<br>9.80 | 16.93,<br>16.80 | 6.71,<br>6.80 | — | 58.37 | 9.80 | 17.24 | 6.81 | — |
| $C_2H_5OCH_2-CH_2-CCl=CH-CH_2N(C_2H_5)_2$ | 100.5—103 ( 5)<br>109.2—111.5 (10) | 0.9514 | 1.4569 | 62.90 | 62.64 | 60.57,<br>60.54 | 10.10,<br>10.07 | 15.38,<br>15.28 | 6.40,<br>6.47 | —<br>— | 60.61 | 10.09 | 16.14 | 6.37 | — |

The structure of the reaction products of α-halo-ethers and chloroprene was established from data on their selective ozonization, reduction and dehalogenation with alcoholic alkali.

1. Decomposition of the ozonides of the addition products of chloroprene and α-chloromethyl ethyl ether gave β-ethoxypropionic acid and a smaller amount of chloroacetic acid. The reaction products also contained chloroacetaldehyde (determined as the 2,4-dinitrophenylhydrazone) but no ethoxypropionaldehyde. These data indicate that the substance has a 1,4-structure and most probably formula (VI).

2. The 1,4-structure of the addition products of α-chloro- and α-bromo-ethers and chloroprene is also supported by experiments on determining primary allyl chlorine in them, by the Sommelet-Leets method [6, 7]. The reaction proceeded very slowly in this case although in two days it was 90-95% complete.

3. Formula (VI) is supported by experiments on the effect of zinc dust in an aqueous-alcohol medium on the addition products of α-chloromethyl and α-chloromethyl ethyl ethers. This gave only small amounts of liquids with low boiling points, which, judging by the infrared spectra, either contain none or very minute quantities of allene ethers which are the probable reduction products of substances with formula (V).

4. According to formula (VI) the addition products of α-halo-ethers and chloroprene very readily exchange one of the halogen atoms for a hydroxyl, ether or amino group. When treated with alcoholic alkali in the cold they gave a series of diethers of an unsaturated, chlorine-containing glycol and when treated with diethylamine— the corresponding ethers of diethylaminochloropentenol. The constants of these substances are given in Table 2.

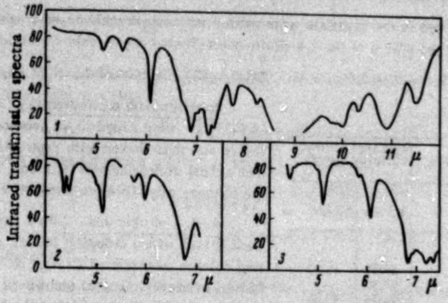
It was thus established that the addition of α-halo-ethers occurred exclusively or almost exclusively in accordance with the assumed polarization of the chloroprene molecule in the 1,4-position.

Heating diethers of chloroglycol and ethers of diethylaminopentenol with solutions of KOH in Cellosolve eliminated hydrogen halide to form a mixture of acetylene, allene and diene compounds. This structure for the dehalogenation products is based on a study of their infrared spectra (figure); in them we detected frequencies characteristic of an acetylene bond (4.42μ) and an allene (5.09μ) and a 1,3-diene(5.97-6.04μ) system. These mixtures were not studied in greater detail.

The α-chloro- and α-bromo-ethers were prepared by the action of gaseous hydrogen halides on a suspension of paraformaldehyde in the appropriate alcohol and were purified by distillation at normal pressure. The yields were 60-80% (on paraformaldehyde).

The properties of the α-chloro- and α-bromo-ethers we prepared are given in Table 3. Ethers 4, 6, 10-12 are described for the first time. The boiling points of the rest agreed with literature data.

The α-halo-ethers were reacted with chloroprene in a liter, four-necked, round-bottomed flask, fitted with a reflux condenser, a thermometer, a dropping funnel and a stirrer with divergent paddles. Stirring was



Infrared transmission spectra. 1) Low-boiling fraction, formed by the action of zinc dust on the product of adding chloromethyl ethyl ether, 2) substance formed by heating the product of adding chloromethyl methyl ether with KOH in Cellosolve, 3) substance formed under the same conditions from the unsaturated diethylaminochloro-ether (R = $CH_3$).

maintained at such a rate that the reading on the thermometer in the flask with the reaction mixture, rapidly reached the reading of a thermometer in the bath cooling the flask. Into the flask was placed zinc chloride or bromide (0.2 g) and then a mixture of 0.5 mole of chloroprene and 0.5 mole of α-halo-ether was added. The reaction mixture, which was first cooled to 0°, was gradually heated to room temperature. The beginning of the reaction was characterized by the appearance of a color at the point of contact with the catalyst and a rise in temperature. The latter was kept at 40-50° by external cooling. At the end of the exothermic process, the mixture was heated for half an hour at 65-70°. The absence of condensate dripping from the reflux condenser, indicated the end of the reaction. Then the contents of the flask were diluted with ether. The ether solution was washed with water containing ammonium oxalate (for the most efficient removal of the catalyst), dried with potash and distilled. The constants, yields and analytical data for the substances obtained are given in Table 1.

TABLE 3

| Expt. No. | Substance | Boiling point | Yield (in %) |
|---|---|---|---|
| 1 | $CH_2Cl—OCH_3$ | 59.5—60° | 82 |
| 2 | $CH_2Cl—OC_2H_5$ | 81.9—82 | 81 |
| 3 | $CH_2Cl—OC_3H_7$ | 108.5—109.5 | 75 |
| 4 | $CH_2Cl—OC_3H_7$-iso | 101.6—101.7 | 58 |
| 5 | $CH_2Cl—OC_4H_9$ | 132—134 | 78 |
| 6 | $CH_2Cl—OC_4H_9$-iso | 122—124 | 75 |
| 7 | $CH_2Br—OCH_3$ | 87.3—88 | 79 |
| 8 | $CH_2Br—OC_2H_5$ | 109.1—109.9 | 80 |
| 9 | $CH_2Br—OC_4H_7$ | 132—134 | 75 |
| 10 | $CH_2Br—OC_3H_7$-iso | 122.2—122.6 | 67 |
| 11 | $CH_2Br—OC_4H_9$ iso | 154.3—156.0 | 77 |
| 12 | $CH_2Br—OC_4H_9$-iso | 144.4—146.2 | 76 |

Ozonization. The product of adding chloromethyl ethyl ether to chloroprene (10.44 g) was ozonized in ethyl chloride. The ozonide was decomposed with water at a temperature of 80°. The solution was neutralized with sodium bicarbonate and freed from aldehydes by partial distillation in vacuum. The residue was acidified with 2 N sulfuric acid and extracted with ether. After removal of the ether, the acids were fractionated at 10 mm. Two fractions were collected - 1st with b.p. 96-98°, 2.5 g; 2nd with b.p. 98-106°, 4.2 g.

The first fraction was found to contain chloroacetic acid, which was isolated as phenoxyacetic acid (0.12 g, which corresponded to 0.075 g of chloroacetic acid). The m.p. was 98° and a mixed sample melted at 98° [8].

A second distillation of the 2nd fraction yielded a product with b.p. 118-120° (20 mm), which contained about 85% of ethoxypropionic acid, together with chloroacetic acid, which was obvious from the analysis data.

Found %: C . 47.57, 47.69; H 7.78, 7.84; $OC_2H_5$ 33.1, 33.9. $C_5H_{10}O_3$. Calculated %: C 50.83; H 8.53; $OC_2H_5$ 38.14. $C_2H_3O_2Cl$. Calculated %: C 25.42; H 3.20.

The aldehydes contained in the distillate were treated with a hydrochloric acid solution of 2,4-dinitrophenylhydrazine. We obtained 0.51 g of the 2,4-dinitrophenylhydrazone of chloroacetaldehyde.

Found %: N 21.42, 22.01; Cl 13.70, 13.85. $C_8H_7O_4N_4Cl$. Calculated %: N 21.66; Cl 13.71.

TABLE 4

| $RO-CH_2-CH_2-CCl=CH-CH_2Hlg$ | | Yield of primary chloride (in %) | |
|---|---|---|---|
| R | Hlg | after 3.5 hrs | after 50 hrs |
| $CH_3$ | Cl | 79.49 | 85.80 |
| $CH_3$ | Br | 97.20 | — |
| $C_2H_5$ | Cl | 96.04 | 97.26 |
| $C_3H_7$ | Cl | 87.23 | 99.02 |
| $C_3H_7$ | Br | 84.55 | 97.88 |
| $C_3H_7$- iso | Cl | 86.24 | 101.14 |
| $C_3H_7$- iso | Br | 91.27 | 92.43 |

Reaction with urotropine [7]. Samples of the ethers (0.5-1.0 g) were added to an acetone solution of potassium iodide and then shaken with urotropine for 3.5 and 50 hours. The excess urotropine was titrated. The data obtained on the primary allyl chloride contents are presented in Table 4.

Action of zinc dust. Into a liter, round-bottomed flask, fitted with a dropping funnel, a stirrer and a fractionating column, was placed 22.5 g (250% excess) of zinc dust, 150 ml of methyl alcohol and 50 ml of water. The mixture was heated to boiling and stirred, while 25 g of the addition product of chloromethyl ethyl ether and chloroprene was added dropwise. After removal of the first distillate at 70-74° (150 ml), 200 ml of water was added to the reaction flask and then a second distillate (190 ml) was collected. The first distillate was diluted with water and distilled until the moment when a clear (on dilution with water) distillate appeared. Saturation of the distillate with calcium chloride gave an oil (7.5 g). Further distillation of the aqueous layer and subsequent salting out with calcium chloride yielded a further 0.3 g of oil.

Distillation of the oil gave a low-boiling fraction with b.p. 117-118° (3.3 g), $d_4^{20}$ 0.7879, $n_D^{20}$ 1.4098.

Found %: C 76.40, 76.60; H 13.08, 13.04.

These data do not correspond to the formula $C_7H_{12}O$ or to the formula $C_7H_{14}O$. The spectrum of the substance is given in the figure (curve 1).

Dilution of the second distillate precipitated a heavy oil containing the original ether.

Action of alcoholic alkali. a) To a solution of 0.1 mole of the addition products of chloroprene and α-chloro- or α-bromo-ether was added a 15% alcohol solution of KOH (100 ml). When the mixture had stood for 12 hours, the precipitate of KCl or KBr was filtered off and washed with dry ether. The filtrate was diluted with water. The lower (aqueous) layer was extracted with ether. The combined ether extracts and the upper layer were washed with saturated calcium chloride solution. After being dried over $CaCl_2$, the ether was distilled at normal pressure and the residue in vacuum. The yield of glycol diether was about 80-85% (about 98% according to KCl or KBr). The properties of the compounds obtained and the analytical data are presented in Table 2.

b) 10.4 g of KOH (two-fold excess) in Cellosolve (90 ml) was added to 15 g of 1,5-dimethoxy-3-chloropentene-2. The mixture was heated on a boiling water bath for 25 minutes, diluted with water and extracted with ether.

After normal treatment of the ether layer by distillation in vacuum, we obtained a substance with the following constants.

B.p. 65-67° (10 mm), 86-94.5° (50 mm). Yield 37% (according to KCl 68%).
Found %: C 65.52; H 9.21. $C_7H_{12}O_2$. Calculated %: C 65.62; H 9.44.

The infrared spectrum of the substance is given in the figure (curve 2).

c) The action of KOH in Cellosolve on 1,5-diethoxy-3-chloropentene-2 gave a 56% yield (87% according to KCl) of a substance with the following constants: b.p. 83-86° (10 mm), 121-122° (50 mm).

Reaction with diethylamine. The addition products of chloroprene and α-halo-ethers were mixed with a two-fold excess of diethylamine with cooling. A 30% solution of NaOH was added to the mixture obtained. The upper layer was extracted with ether. The ether extracts were dried over KOH and vacuum distilled. The yield of amines was 80-85%.

The constants and analytical data are presented in Table 2.

When 16.1 g of 1-diethylamino-3-chloro-5-ethoxypentene-2 was heated with 11 g (three-fold excess) of KOH in Cellosolve for 1.5 hours, we isolated 4.9 g (85%) of KCl. Distillation in vacuum yielded a substance with b.p. 102-103° (10 mm). The yield was 59%.

Found %: C 71.90; H 11.70; N 7.59, 7.84. $C_{11}H_{21}ON$. Calculated %: C 72.13; H 11.55; N 7.64.

The infrared spectrum of the substance is given in the figure (curve 3).

## SUMMARY

1. The reaction of chloroprene with α-chloro- and α-bromo- ethers $CH_2Hal - OR(R = CH_3, C_2H_5, C_3H_7$ and iso-$C_3H_7$ was investigated.

2. It was established that the addition occurs mainly at the 1,4-position, with the halogen tending towards the fourth atom of the diene system.

3. From the addition products of halo-ethers and chloroprene we prepared halogen-containing unsaturated diethers and amino ethers. The effect of KOH in cellosolve on them was investigated.

## LITERATURE CITED

[1] B. A. Arbuzov, Article in the Coll. "Reactions and Methods of Investigation", GNTIKhL (State Sci. Tech. Press, Chem. Lit.) (1952).

[2] A. N. Pudovik and B. A. Arbuzov, Bull. Acad. Sci. USSR, Div Chem. Sci., 1946, 427.

[3] A. N. Pudovik, Ibid., 1948, 321, 529; A. N. Pudovik, V. I. Nikitina and S. Kh. Aigistova, J. Gen. Chem., 19, 279 (1949).*

[4] A. N. Pudovik and N. Altunina, J. Gen. Chem. 26, 1635 (1956).*

[5] A. A. Petrov and K. V. Leets, J. Gen. Chem. 26, 1113 (1956).*

[6] R. Sommelet, C.r. 157, 852 (1913).

[7] K. V. Leets, A. I. Piliavskaia and M. I. Korovina, J. Gen. Chem., 27, 2969 (1957).*

[8] Dict. Org. Cmpds., III, 373 (1949).**

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*See C. B. Translation.

**In Russian.

# CONJUGATED SYSTEMS

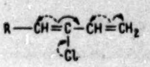
## LXXXVIII.* CONDENSATION OF 3-CHLORO-1,3-PENTADIENE AND 3-CHLORO-1,3-HEXADIENE WITH PROPARGYLALDEHYDE AND PROPIOLIC ACID

E. A. Leporskaia and A. A. Petrov

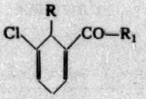
In a series of recently published papers on the direction of the diene synthesis the problem of the differing influence exerted by several dissimilar substituents on the diene system has been discussed quite inadequately [1-3]. At the same time, in the case of benzene derivatives definite arrangements of the substituents based on the magnitude of their orienting influence were established long ago [4]. We undertook to study this problem on the examples of condensing 3-chloro-1,3-pentadiene with propiolic acid and 3-chloro-1,3-hexadiene with propargylaldehyde and the same acid.

The aromatic analog of 3-chloro-1,3-pentadiene is o-chlorotoluene. In the bromination and nitration of the latter the methyl group shows a smaller orienting influence than the chlorine atom [5, 6]. In its substitution reactions the analog of 3-chloro-1,3-hexadiene is o-chloroethylbenzene, but here we were unable to find the corresponding data of the orienting influence of substituents in the literature.

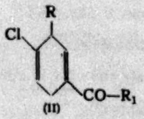
Our experiments revealed that in the diene synthesis reactions involving both of the above-named halo derivatives the formation of two possible addition products (I and II) is observed in all cases, in which connection the main direction of the reaction is that which is determined by the presence of the alkyl group.



Determining the amounts of isomers with a m-alkyl group and an oxygen-containing radical (II) in the reaction products did not present any difficulties. These isomers when oxidized with dilute nitric acid give the known 4-chloroisophthalic acid in good yields. At the same time, isomer (I) suffers decomposition when oxidized.



(I)



(II)

We judged the relative amounts of the two isomers by the results of the chromatographic separation of their mixture and by the amount of 4-chloroisophthalic acid formed in the oxidation of the whole mixture.

The chromatographic separation of the mixed acids obtained as products in the condensation of chloropentadiene with propiolic acid enabled us to isolate two chloromethyldihydrobenzoic acids with melting points of 122-124° and 167-169°, respectively in the ratio of approximately 3 : 1. The first of these acids when oxidized does not give an aromatic acid, while the second yields 4-chloroisophthalic acid. On this basis the second acid was assigned the formula of 4-chloro-3-methyl-$\Delta^{1,4}$-dihydrobenzoic acid. Only the formula of 3-chloro-2-methyl-$\Delta^{2,6}$-dihydrobenzoic acid remained for the first acid.

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* Diene compounds. LXVII. Diene synthesis involving halodienes. XI.

Chromatographing of the mixed acids obtained in the condensation of the chlorohexadiene with propiolic acid gave acids with melting points 103-105° and 153-154°, also respectively in the ratio of approximately 3:1. Oxidation of the high-melting acid gave 4-chloroisophthalic acid, on which basis the structure of 4-chloro-3-ethyl-$\Delta^{1,4}$-dihydrobenzoic acid was assigned to this isomer. Oxidation of the second isomer with nitric acid did not give an aromatic acid, and consequently only the formula of 3-chloro-2-ethyl-$\Delta^{3,6}$-dihydrobenzoic acid could be assigned to it, which was confirmed by its oxidation with potassium permanganate, where the known 3-chlorophthalic acid was obtained in very small yield. The dehydrogenation of the 3-chloro-2-ethyldihydrobenzoic acid over palladium apparently gave the previously unknown 3-chloro-2-ethylbenzoic acid.

The condensation of the chlorohexadiene with propargylaldehyde gave a chloroethyldihydrobenzaldehyde with a narrow boiling range. Treatment of the latter with methylmagnesium iodide gave a secondary alcohol, which also distilled in a narrow boiling range. However, when this aldehyde was oxidized with silver oxide we obtained a mixture of two of the acids discussed above with m.p. 103-104° and 152-154°. Only 4-chloroisophthalic acid is obtained when the mixture of aldehydes was oxidized with nitric acid. Oxidation with alkaline potassium permanganate solution gave, besides 4-chloroisophthalic acid, also a small amount of o-ethylbenzoic acid, formed by the cleavage of hydrogen chloride from the low-melting chloroethyldihydrobenzoic acid.

The presented experimental data indicate that orientation in the diene synthesis is evidently determined by somewhat different factors than is the orientation in reactions involving substitution in the benzene ring. In the case investigated by us the alkyl group exerts a greater influence on the reaction result than does the chlorine atom. At the same time, the reverse situation is observed in the case of 3-chloro-2-methyl-1,3-butadiene [3]. This is apparently due to the fact that steric factors play a greater role in the diene synthesis, in the given case the greater availability of the $CH_2=$ group when compared with the other end of the molecule.

## EXPERIMENTAL

All of the condensations were run in toluene solution in sealed glass tubes at 110-120° for 10 hours in the presence of hydroquinone.

Condensation of 3-chloro-1,3-pentadiene with propiolic acid. From 5.7 g of the chloropentadiene and 2.5 g of propiolic acid we obtained 5.4 g (88%, based on the acid) of crystalline condensation products contaminated with polymer. The polymers were precipitated by adding water to a hot solution of the condensation products in alcohol. 4-Chloro-3-methyl-$\Delta^{1,4}$-dihydrobenzoic acid with m.p. 167-169° (0.52 g) was isolated when the obtained mixture of chloromethyldihydrobenzoic acids was recrystallized 6 times from toluene. Further recrystallizations did not change the melting point.

Found %: Cl 20.36 equiv. 170.0. $C_8H_9O_2Cl$. Calculated %: Cl 20.54. equiv. 172.6.

Oxidation of the substance with 20% nitric acid in sealed tubes at 160° for 10 hours gave an 80% yield of 4-chloroisophthalic acid with m.p. 291.5-293° (cor.) [7].

Found %: Cl 17.60 equiv. 100.0. $C_8H_5O_4Cl$. Calculated %. Cl 17.68. equiv. 100.3.

Repeated passage of the solutions obtained after removal of most of the 4-chloro-3-methyldihydrobenzoic acid through a column of aluminum oxide enabled us to isolate 3-chloro-2-methyl-$\Delta^{3,6}$-dihydrobenzoic acid with m.p. 122-124° (1.57 g).

Found %: Cl 20.11. equiv. 170.0 $C_8H_9O_2Cl$. Calculated %: Cl 20.54. equiv. 172.6.

Oxidation of the substance with 20% nitric acid gave acetic acid and traces of a substance with m.p. 264°.

Condensation of 3-chloro-1,3-hexadiene with propiolic acid. From 3.2 g of the chlorohexadiene and 1.5 g of propiolic acid we obtained 2.8 g (70%) of crystalline condensation products. In a second experiment we obtained 4.7 g (73%) of the same products from 5.8 g of the chlorohexadiene and 2.4 g of propiolic acid.

Recrystallization from toluene and chromatographic separation of the mixture led to the isolation of two acids.

1) 4-Chloro-3-ethyl-$\Delta^{1,4}$-dihydrobenzoic acid with m.p. 153-155°.

Found %: Cl 19.14. equiv. 185.0, 189.0. $C_9H_{11}O_2Cl$. Calculated %: Cl 19.00. equiv. 186.6.

Oxidation of the substance with 20% nitric acid gave 4-chloroisophthalic acid with m.p. 293.5-295.5° (cor.).

2) 3-Chloro-2-ethyl-$\Delta^{2,6}$-dihydrobenzoic acid with m.p. 103-105 (three times the amount of (1)).

Found %: C 58.01, 58.25; H 6.19, 6.23; Cl 19.24, $C_9H_{11}O_2Cl$. Calculated %: C 57.92; H 5.94, Cl 19.00.

Oxidation of the substance with 20% nitric acid gave acetic acid.

Oxidation of the original mixture of acids (1.8 g) with potassium permanganate (6.32 g) in alkaline solution (2.28 g of KOH in 40 ml of water) with heating on the water bath until the solution became colorless gave two acids–3-chlorophthalic acid with m.p. 186° [6] (about 0.01 g) and 4-chloroisophthalic acid (0.47 g), together with some lower melting acids (about 0.1 g).

Condensation of 3-chloro-1,3-hexadiene with propargylaldehyde. The mixture obtained from the condensation of 17 g of the chlorohexadiene and 10 g of propargylaldehyde was first steam-distilled and then the oil was fractionally distilled in vacuo to give 8 g (32%) of mixed chloroethyldihydrobenzaldehydes.

B.p. 130-131° (20 mm), $d_4^{20}$ 1.1314, $n_D^{20}$ 1.5230, $MR_D$ 46.07; calc. 45.51.
Found %: Cl 20.57. $C_{15}H_{11}OCl$. Calculated %: Cl 20.78.

2,4-Dinitrophenylhydrazone. M.p. 202-204° (from alcohol).

Found %: N 15.87. $C_{15}H_{15}O_4N_4Cl$. Calculated %: N 15.97.

Oxidation of the condensation products with 20% nitric acid at 160° for 10 hours gave a crystalline product, from which 4-chloroisophthalic acid with m.p. 293-294° was isolated after three recrystallizations.

Oxidation of the aldehyde (6.6 g) with potassium permanganate (30.2 g) in alkaline solution (5 g KOH in 50 ml of water) gave acetic acid, an apparent polymer of the aldehyde and 3 g of mixed solid acids, about 80% of which was 4-chloro-isophthalic acid with m.p. 294°. Chromatographic separation of the acids in ethyl alcohol solution enabled us to isolate a small amount of o-ethylbenzoic acid with m.p. 66-68°.

Oxidation of the aldehyde with silver oxide in alkaline medium gave, together with the polymer, a mixture of acids, which was separated by chromatographing into two acids with m.p. 103-104° (60-70% of the mixture) and 152-154°, respectively. Both acids failed to depress the melting point when mixed with the similar substances obtained in the condensation of 3-chloro-1,3-hexadiene with propiolic acid.

Dehydrogenation of the first acid (0.17 g) by heating with palladium black gave, probably, 3-chloro-2-ethylbenzoic acid with m.p. 126-128°. The substance was not studied more closely.

Reaction of 7.5 g of the mixed chloroethyldihydrobenzaldehydes with a solution of methylmagnesium iodide in ether (20% excess) gave a mixture of two secondary alcohols–3-chloro-2-ethyl-$\Delta^{2,6}$-dihydro-$\alpha$-phenylethyl and 4-chloro-3-ethyl-$\Delta^{1,4}$-dihydro-$\alpha$-phenylethyl alcohols.

B.p. 129-130° (10 mm), $d_4^{20}$ 1.1096, $n_D^{20}$ 1.5185, $MR_D$ 51.02; calc. 51.64.
Found %: Cl 18.74. $C_{10}H_{15}OCl$. Calculated %: Cl 18.99.

## SUMMARY

1. The condensation of 3-chloro-1,3-pentadiene with propiolic acid and of 3-chloro-1,3-hexadiene with propiolic acid and with propargylaldehyde were investigated.

2. It was shown that a mixture of the two possible isomeric chloroalkyldihydrobenzoic acids or benzaldehydes is formed in all cases as a result of condensation, with the isomers having an o-alkyl group and an oxygen-containing radical present in predominant amount.

## LITERATURE CITED

[1] A. A. Petrov, and co-workers, J. Gen. Chem. 11, 309, 661, 665 (1941); 17, 497, 1295, 2228 (1947); 18, 424, 1125, 1781 (1948); 22, 591 (1952);* 24, 298 (1954);* 25, 517, 739 (1955);* 26, 2744, 2995 (1956);* J. Gen. Chem. Suppl. I, 369 (1953).

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*See C. B. Translation.

[2] I. N. Nazarov, A. I. Kuznetsova and N. V. Kuznetsov, J. Gen. Chem. 25, 88 (1955).*

[3] K. Alder, K. Heimbach and K. Neufang, Lieb. Ann. 586, 138 (1954).

[4] M. I. Kabachnik, Prog. Chem. 17, 96 (1948).

[5] J. B. Cohen and C. J. Smithells, J. Chem. Soc. 105, 1910 (1914).

[6] J. P. Wibaut, Rec. trav. chim. 32, 286 (1913).

[7] Dictionary of Organic Compounds [In Russian.] Vol. I, pp. 487, 522 (1949).

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Manufacture

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*See C. B. Translation.

# CONJUGATED SYSTEMS

## LXXXIX.* INFLUENCE OF VARIOUS FACTORS ON THE YIELD OF GERANYL CHLORIDE IN THE REACTION OF ISOPRENE WITH ITS HYDROCHLORIDES

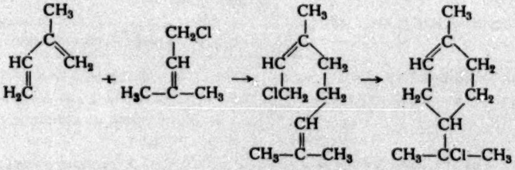
A. A. Petrov, Kh. V. Bal'ian, Iu. I. Kheruze, E. Iu. Shvarts
and L. L. Cherenkova

The possibility of adding halo derivatives to diene hydrocarbons was first briefly mentioned relative to the addition of tert-butyl halides and allyl halides [1]. A more detailed study of the reaction of diene hydrocarbons with alkyl halides was made in our laboratory [2]. It was established that in the presence of zinc halides the primary, secondary and tertiary alkyl halides add to diene hydrocarbons, in which connection the reaction rate increases in the given order. Primary addition products (1: 1 ratio) were isolated only in the case of the reaction of tert-alkyl halides with butadiene; mixtures of the higher telomers were obtained in the other cases. Some experiments were also made on the reaction of diene hydrocarbons with unsaturated halo derivatives, and successful results were obtained here also [3, 4].

The data obtained in the addition of prenyl chloride (1-chloro-3-methyl-2-butene) to isoprene with the formation of geranyl chloride deserved special attention. The fact that synthetic geranyl chloride was obtained in good yield here opened up a broad vista for both the perfume and vitamin industries. This circumstance caused a number of laboratories, including ours, to undertake a detailed study of the reaction of diene hydrocarbons with their hydrochlorides in order to determine the possibility of obtaining the optimum yields of geranyl chloride and its homologs [5, 6].

The addition of isoprene hydrochlorides to isoprene yields a complex mixture of halo derivatives with the composition $C_5H_9-(C_5H_8)_n-Cl$. In this paper we investigated only the fraction of terpene chlorides with composition $C_{10}H_{17}Cl$ (n = 1 ).

Theoretically the formation of 12 aliphatic and 2 alicyclic terpene chlorides could be expected from isoprene and its two hydrochlorides. It was unequivocally shown [6] that both geranyl chloride (conversion to citral) and terpinyl chloride (conversion to α-terpineol) are present in this mixture. Both mentioned compounds are the products of the addition of prenyl chloride to isoprene, in which connection the terpinyl chloride is formed from geranyl chloride by isomerization due to the double bond present.



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* Diene compounds. LXVIII. Reaction of dienes with halo derivatives. IV.

Besides these products, the obtained mixture of terpene chlorides can also contain linalyl chloride and a substance arising from the addition of dimethylvinylchloromethane to isoprene, namely the allyl isomer of prenyl chloride. A detailed study of this mixture will be the subject of future investigations.

The results of our experiments on a study of the influence exerted by various conditions on the yield of geranyl chloride are discussed in this communication. The method developed under the direction of K. V. Leets [7] and based on the Sommelet reaction was selected by us as the principal method for determining the amount of primary chlorides of the allyl type in the mixture;

The influence of the following on the yield of geranyl chloride was investigated: 1) nature of the catalyst, 2) nature of the hydrochloride, 3) ratio of the reactants, 4) nature of the solvent, 5) temperature, and 6) degree of conversion.

We tested 15 different compounds as catalysts for this reaction. Of them only the following proved to be effective: stannic chloride, zinc chloride, ferric chloride, aluminum chloride and titanium chloride. Cuprous and cupric chlorides, mercurous and meruric chlorides, the chlorides of cobalt, lead and phosphorus, and also hydrogen chloride, zinc sulfate, benzoyl peroxide and azobisisobutyronitrile failed to show any catalytic activity.

The most effective catalyst is anhydrous stannic chloride. It causes telomerization to proceed at room temperature and lower, using concentrations of the order of a tenth of a percent on the weight of reaction mixture (Table 1, Expts. 1-19).

TABLE 1

Influence of Telomerization Reaction Conditions on Yield of Geranyl Chloride

| Exp. No. | Catalyst | Hydrochloride | Degree of conversion (in %) | Density increase Δd | Solvent | Temp | Am't of telomer (in g) | Desired fraction (in % of telomer) | Geranyl chloride | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | Am't in desired fraction (in %) | yield (in %) |
| 1 | $SnCl_4$ | 1.4 | 25 | 0.041 | $CH_2Cl_2$ | 10° | 24.2 | 48 | 54.5 | 26.0 |
| 2 | | | 29 | 0.048 | $CH_3NO_2$ | 10 | 28.5 | 33 | 56.8 | 18.5 |
| 3 | | | 31 | 0.051 | $CH_2Cl_2$ | 10 | 30.0 | 40 | 52.8 | 21.0 |
| 4 | | | 31 | 0.051 | $CH_2Cl_2$ | 25 | 30.4 | 44 | 47.9 | 21.0 |
| 5 | | | 32 | 0.045 | $C_8H_{18}$ | 10 | 31.5 | 40 | 46.4 | 18.3 |
| 6 | | | 33 | 0.050 | $CH_2Cl_2$ | 35 | 32.5 | 42 | 48.8 | 20.6 |
| 7 | | | 34 | 0.064 | Without solvent | 30 | 33.0 | 35 | 39.8 | 19.8 |
| 8 | | | 35 | 0.053 | $CH_3NO_2$ | 10 | 34.0 | 32 | 56.8 | 17.9 |
| 9 | | | 37 | 0.048 | $CH_2Cl_2$ | 35 | 36.8 | 38 | 48.1 | 18.4 |
| 10 | | | 39 | 0.055 | $CH_3NO_2$ | 10 | 38.3 | 31 | 54.3 | 17.0 |
| 11 | | | 41 | 0.045 | $C_8H_{18}$ | 10 | 39.8 | 35 | 40.7 | 14.4 |
| 12 | | | 43 | 0.058 | $C_8H_{18}$ | 15 | 42.3 | 29 | 39.9 | 11.5 |
| 13 | | | 44 | 0.072 | $CH_2Cl_2$ | 38 | 42.9 | 30 | 41.6 | 12.7 |
| 14 | | | 47 | 0.073 | $CH_2Cl_2$ | 10 | 45.9 | 29 | 43.7 | 12.7 |
| 15 | | 1.2 | 14 | 0.041 | $CH_2Cl_2$ | 40 | 13.4 | 54 | 59.0 | 32.0 |
| 16 | | | 23 | 0.056 | $CH_2Cl_2$ | 10 | 22.6 | 45 | 47.7 | 25.7 |
| 17 | | | 25 | 0.064 | $CH_2Cl_2$ | 10 | 25.6 | 45 | 55.5 | 24.8 |
| 18 | | | 32 | 0.069 | $CH_2Cl_2$ | 30 | 31.6 | 44 | 50.1 | 21.8 |
| 19 | | | 43 | 0.077 | $C_8H_{18}$ | 10 | 42.0 | 30 | 42.4 | 12.8 |
| 20 | $SnCl_4 \cdot 5H_2O$ | 1.4 | 32 | 0.045 | $CH_2Cl_2$ | 40 | 31.6 | 44 | 44.3 | 19.6 |
| 21 | $SnCl_4 \cdot 5H_2O$ | | 44 | 0.075 | $CH_2Cl_2$ | 40 | 47.5 | 41 | 33.5 | 13.8 |
| 22 | $ZnCl_2$ | | 33 | 0.037 | $C_8H_{18}$ | 40 | 32.4 | 60 | 34.1 | 20.6 |
| 23 | $ZnCl_2$ | | 51 | 0.061 | $CH_2Cl_2$ | 40 | 49.7 | 53 | 26.9 | 14.2 |

Stannic chloride crystal hydrate, both as a solid and in alcohol solution, is also an effective telomerization catalyst; however, its activity is lower than that of the anhydrous stannic chloride, and consequently it has to be used in larger amounts and the reaction has to be run at 35-40° (Expts. 20 and 21). That it is possible to use this catalyst is indicated by the fact that small amounts of moisture do not interfere with the reaction.

A disadvantage of stannic chloride is the fact that it favors the formation of substantial amounts of higher telomerization products. In the presence of this catalyst it is necessary to stop the process when only 20-30% of the isoprene has been consumed in order to obtain geranyl chloride in a yield of about 25% on consumed isoprene.

Zinc chloride is also an active telomerization catalyst. Its use in alcohol solution at 40° makes it possible to substantially improve the yield of terpene chlorides at the expense of reducing the yield of higher telomers; however, the yield of geranyl chloride based on isoprene remains the same as in the case of using stannic chloride (Expts. 22 and 23). The yield of terpene chlorides increases as the amount of this catalyst is increased.

Ferric chloride is an active telomerization catalyst (anhydrous, as solid crystal hydrate, and in alcohol solution). The yield of terpene chlorides in the presence of this catalyst is lower than in the presence of the first two discussed.

Aluminum chloride was used in ether solution. The reaction went only on heating. Strong tarring of the products occurred during distillation.

The reaction with titanium chloride goes slowly. It is necessary to use larger amounts of this catalyst.

The presented data caused us to choose two catalysts—stannic chloride (either anhydrous or as the crystal hydrate) and zinc chloride – for further studies.

The two isomeric isoprene hydrochlorides react at a different rate with isoprene in the telomerization reaction. Prenyl chloride reacts several times faster than does dimethylvinylchloromethane. However, for the same degree of conversion, the yield of geranyl chloride is not affected by this (Expts. 11, 19; 3, 4, 18; 1, 16, 17). Since the telomerization reaction in the presence of metal chlorides undoubtedly has an ionic character, and since the two isomeric isoprene hydrochlorides have the same common ion, then the addition products should have approximately the same composition independent of the structure of the starting halo derivative, which is what was actually observed. The ratio of isoprene to its hydrochlorides was varied from 1 : 0.5 to 1 : 2. The yield of terpene chlorides increased somewhat as the amount of starting chloride was increased, but this increase was less than the increased consumption of hydrochloride.

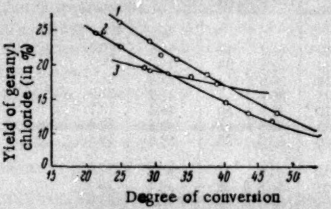

Fig. 1. Influence of the nature of the solvent and the degree of telomerization on the yield of geranyl chloride. 1) methylene chloride, 2) n-octane, 3) nitromethane

Compounds with sharply different polar properties were tested as solvents: n-octane, methylene chloride and nitromethane. For the same small degree of conversion the nature of the solvent was practically without effect on the yield of geranyl chloride. The best results were always obtained in methylene chloride. In nitromethane a less sharp reduction in the yield of geranyl chloride was observed as the degree of telomerization was increased (see Fig. 1). Approximately the same yields of geranyl chloride were also obtained when operating without a solvent, but it is difficult to regulate the reaction rate in the absence of a solvent(Expts. 12 and 13; 2, 4, and 5; 7, 8, and 9).

Temperature influences only the reaction rate (Expts. 3, 4 and 6; 13 and 14).

The single factor that strongly influences the yield of primary terpene chlorides is the degree of conversion. When the degree of conversion is 25% the yield of geranyl chloride is about 25%, when the degree of conversion is 30% the yield drops to 20% and, finally, when the degree of conversion is 45% the total yield of geranyl chloride is only 12-13% (Expts. 1, 3, and 4; 6, 9, and 13; 11 and 12).

The presented data permit the conclusion that to obtain a geranyl chloride suitable for conversion to citral it is possible to use a mixture of the two isomeric isoprene hydrochlorides. If together with geranyl chloride it is desired to use the higher telomers, for example farnesyl chloride, then stannic chloride is the best catalyst; it proves feasible to use only the cyclic terpene chlorides, then zinc chloride possesses certain advantages. In all cases the degree of conversion should be low. As regards the other conditions (temperature, solvents, reactant ratios), then they exert a smaller influence on the yield of geranyl chloride.

Since regulating the degree of conversion determines the success of synthesizing geranyl chloride from isoprene, we undertook a detailed study of methods to arrest the telomerization reaction at a given stage. Earlier it had been proposed to terminate the telomerization reaction by adding water or aqueous salt solutions to the reaction mixture [3, 5]. This method made subsequent workup extremely difficult and caused gross contamination of the end products by substances formed as a result of their hydrolysis. Much better results were achieved when solid, liquid and gaseous inorganic and organic amino compounds were used as agents to arrest the telomerization reaction [8]. Compounds of the indicated type react with the catalyst to yield complexes that are both devoid of catalytic activity and insoluble in the mixture of telomers. The addition products of amines to stannic chloride belong to the class of tetraacidoamino compounds with the tin having a coordination number of 6. Zinc chloride yields similar compounds with a coordination number of 4 [9]. As "quenching agents" we tested ammonia (both as a gas and on activated carbon), ammonium carbonate, diethylamine, triethylamine, tribenzylamine, aniline, methylaniline, pyridine, urea, thiourea, melamine, etc. All of the enumerated compounds terminate the telomerization reaction, but at a different rate. Under laboratory conditions we found liquid "quenching agents" to be the most satisfactory. The yield of geranyl chloride does not depend on the nature of the "quenching agent".

In order to characterize in more detail the products obtained in the telomerization of isoprene with its hydrochlorides we fractionally distilled the products obtained in three of the experiments. From these experiments it can be seen that the major portion of the terpene chlorides distills in a 5-7° range. We took the main fractions of the terpene chloride specimens and determined both their infrared spectra and the amount of geranyl chloride contained in them. In the experiments using stannic chloride the main terpene chloride fraction contained about 50% geranyl chloride, while in the experiments with zinc chloride the geranyl chloride content was about 25%. In all cases the amount of dienic halo derivatives proved to be greater than the amount of geranyl chloride. Consequently, these fractions contain an isomeric chloride, apparently linalyl chloride.

The infrared spectra of the main fractions from all three experiments proved to be similar. In order to determine the possibility of using these spectra for the qualitative and quantitative determination of the amounts of geranyl, linalyl and terpinyl chlorides in the telomerization products we attempted to prepare these compounds in the pure state from the corresponding alcohols and investigate their infrared spectra. Pure terpinyl chloride was obtained from crystalline synthetic terpineol. We were able to obtain the geranyl chloride only 86% pure. Linalyl chloride could not be isolated in a concentration greater than 50%. A comparison of the spectra of geranyl and terpinyl chlorides led to the conclusion that an intense frequency at 835 $cm^{-1}$ is characteristic for the first compound, and one at about 790 $cm^{-1}$ (doublet) for the second. It should also be mentioned that terpinyl chloride shows much stronger adsorption than geranyl chloride at 1150 $cm^{-1}$. In the spectrum of geraniol the 835 $cm^{-1}$ frequency has a weak intensity. On the contrary, $\alpha$-terpineol, the same as terpinyl chloride, shows strong adsorption at 790 $cm^{-1}$. The spectrum of linalool has intense frequencies at 916 and 988 $cm^{-1}$, characteristic for the vinyl group. Apparently, linalyl chloride should also absorb in this region. Only the higher frequency can be used to determine linalyl chloride, since the frequency in the vincinity of 916 $cm^{-1}$ is also found in the spectrum of terpinyl chloride.

Based on the presented data it becomes possible to make some conclusions relative to the composition of the terpene chlorides obtained as products in the telomerization of isoprene with its hydrochlorides. As can be seen from Fig. 2, all three investigated mixtures contain geranyl chloride (frequency 835 $cm^{-1}$), terpinyl chloride (frequency 790 $cm^{-1}$) and linalyl chloride (frequency 988 $cm^{-1}$). Apparently, these mixtures also contain some other chloride, showing intense absorption around 910 $cm^{-1}$. Based on the ratio of the intensities of the characteristic frequencies it can be concluded that the above three terpene chlorides are formed in close amounts from both isoprene hydrochlorides. The amount of terpinyl chloride in the mixture increases sharply when zinc chloride is used as the catalyst. This conclusion is in agreement with the chemical data.

The infrared spectrum in the regionof 6.060 $cm^{-1}$ can also be used to analyze mixtures of terpene chlorides. As is known, compounds containing the vinyl group have a characteristic frequency ($^{\nu}$Ch overtone) in this region. Terpineol, geraniol and their chlorohydrins do not absorb in this region. Linalool has an intense overtone at 6.060 $cm^{-1}$.

The mixtures of terpene chlorides obtained by telomerization absorbed at 6.060 $cm^{-1}$, and therefore undoubtedly contained the product of the addition of prenyl chloride to isoprene in the 1,2 position, i.e. linalyl

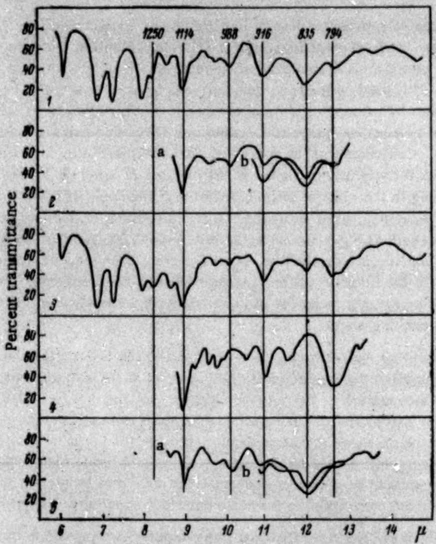

Fig. 2. Infrared spectra of the products obtained in the telomerization of isoprene with its hydrochlorides. 1) prenyl chloride and isoprene in the presence of $SnCl_4$, 2) dimethylvinylchloromethane and isoprene in the presence of $SnCl_4$: a) fraction 79-81° (5 mm), b) fraction 77-79° (5 mm); 3) prenyl chloride and isoprene in the presence of $ZnCl_2$, 4) terpinyl chloride, 5) geranyl chloride; a) geranyl chloride content 86%, b) geranyl chloride content 65%.

chloride. Judging by the intensity of absorption, the amount of the latter in the terpene chlorides obtained by telomerization in the presence of stannic chloride was considerably higher than in the chlorides obtained by telomerization in the presence of zinc chloride.

## EXPERIMENTAL

Hydrochlorination of isoprene. The synthesis of the isoprene hydrochlorides was run in an apparatus fitted with a disc sparger made of Shott glass No. 1. It was observed that both reducing the temperature and adding either ether or small amounts of water to the mixture hasten the process considerably. The ratio of the isomeric hydrochlorides in the final product depends on the conditions used. Raising the temperature, the presence of moisture, and mainly increasing the degree of hydrochlorination, favor the formation of the primary chloride (prenyl chloride). Depending on the indicated factors, this ratio in different experiments varied from 2: 1 to 1: 4 (tertiary: primary hydrochlorides).

After the desired weight increase had been obtained, the mixture of hydrochlorides was vacuum-distilled throug a Widmer column (80 cm). Distillation at atmospheric pressure causes a part of the tertiary hydrochloride to isomerize to the primary. The yield of isomeric hydrochlorides was about 70-80%. The distillation flask always contained a large amount of residue, which was not investigated more closely.

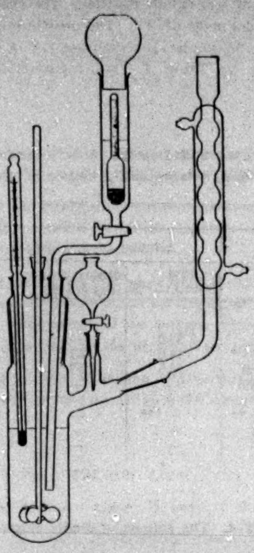

Fig. 3. Apparatus for running the telomerization reaction.

Various constants are given in the literature for the isoprene hydrochlorides. We operated with the following specimens.

3-Chloro-3-methyl-1-butene. B.p. 29-30° (120 mm), $d_4^{20}$ 0.8845, $n_D^{20}$ 1.4190. The amount of primary chloride, by the Sommelet-Leets method, was 10%.

1-Chloro-3-methyl-2-butene. B.p. 39-40° (50 mm), $d_4^{20}$ 0.9290, $n_D^{20}$ 1.4500. Amount of primary chloride 97%.

These constants are in close agreement with those given by Laforgue [10].

Telomerization. The telomerizations were run in the apparatus shown in Fig. 3, which made it possible to control the degree of conversion by the change in the specific gravity of the mixture. For this the liquid was transferred from time to time using a bulb to a vessel containing a hydrometer, and after taking a rapid reading was returned to the reaction vessel. In all of the experiments given in Table 1 the following mixture was taken for reaction: isoprene – 39 g, hydrochloride – 60 g, solvent – 20–25% by volume. The catalyst was added through the funnel. In the experiments with stannic chloride a 5% solution in methylene chloride was used. From 1.5-2 ml of this solution was added to the reaction mixture. In the experiments with zinc chloride a 20% solution in methyl alcohol was used. From 3-5 ml of this solution was added. In the experiments using solid catalysts the latter were added in an amount of 0.1 - 0.2 g through the opening for the dropping funnel. External cooling was used to regulate the reaction rate. With an efficient stirrer this was not difficult.

TABLE 2

Results of the Telomerization of Prenyl Chloride With Isoprene in the Presence of $SnCl_4$ (Isoprene 117 g, prenyl chloride 180 g, degree of telomerization 36%, catalyst $SnCl_4$)

| Fraction No. | Boiling point (5 mm) | Weight (in g) | $d_4^{20}$ | $n_D^{20}$ | % Cl | Amount of | |
|---|---|---|---|---|---|---|---|
| | | | | | | geranyl chloride (in %) | dienic chlorides (in %) |
| 1 | To 76° | 1.0 | — | 1.4735 | — | — | — |
| 2 | 76— 79 | 5.2 | 0.9348 | 1.4745 | 19.65 | 40.5 | — |
| 3 | 79— 82 | 21.8 | 0.9357 | 1.4775 | 20.10 | 52.0 | 73.4 |
| 4 | 82— 90 | 2.0 | 0.9545 | 1.4798 | 19.60 | — | — |
| 5 | 90—105 | 3.5 | 0.9728 | 1.4800 | 18.80 | — | — |
| 6 | 105—140 | 11.0 | — | — | 10.20 | — | — |
| 7 | Residue | 44.5 | — | — | — | — | — |

When the desired increase in the density had been reached (selected experimentally, the density was varied in a range of 0.03) the "quenching agent", in most cases pyridine, was added to the mixture through a dropping funnel. The solid quenching agents work much slower and should be used in larger amounts; however, in a continuous process they are more convenient than the liquid quenching agents.

When the reaction had been terminated and the catalyst separated as the complex, the mixture was fractionally distilled in vacuo. The solvent and reactants were distilled at 50-100 mm. Then the pressure was reduced to 2-3 mm and the portion of the product boiling below 140° was rapidly distilled. The distilled product was refractionated. The terpene chlorides were collected in the range 60-90°. The amount of primary chlorides (geranyl chloride) in this fraction was determined by the Sommelet–Leets method [7]. A total of more than 100 experiments was made; the data of some are given in Table 1. Their reproducibility was satisfactory.

TABLE 3

Results of the Telomerization of Dimethylvinylchloromethane With Isoprene in the Presence of $SnCl_4$ (Isoprene 117 g, dimethylvinylchloromethane 178 g, catalyst $SnCl_4$, degree of telomerization 37%)

| Fraction No. | Boiling point (5 mm) | Weight (in g) | $d_4^{20}$ | $n_D^{20}$ | % Cl | Amount of | |
|---|---|---|---|---|---|---|---|
| | | | | | | geranyl chloride (in %) | dienic chlorides (in %) |
| 1 | To 77° | 2.8 | — | 1.4712 | 17.5 | 33.0 | — |
| 2 | 77—79 | 14.5 | 0.9320 | 1.4760 | 20.55 * | 44.6 | 62 |
| 3 | 79—81 | 10.5 | 0.9360 | 1.4795 | 21.60 | 62.5 | 63 |
| 4 | 81—85 | 3.4 | 0.9443 | 1.4794 | 19.35 | — | — |
| 5 | 85—90 | 1.4 | — | 1.4815 | — | — | — |
| 6 | 90—105 | 2.8 | 0.9798 | 1.4803 | 20.5 ** | — *** | — |
| 7 | 105—140 | 4.5 | — | — | 11.4 | — | — |
| 8 | Residue | 56.5 | — | — | — | — | — |

The data of the larger scale experiments are given in Table 2-4. The amount of dienic chlorides in some of the experiments was established by the Kaufman method.

α-Terpinyl chloride, with b.p. 87-88° (8 mm), $d_4^{20}$ 0.9742, $n_D^{20}$ 1.4840, and chlorine content 20.1%, was obtained from synthetic inactive α-terpineol, with m.p. 33°, b.p. 108-109° (20 mm), $d_4^{20}$ 0.9347, $n_D^{20}$ 1.4818, and melting point of nitrosochloride 112° [11].

TABLE 4

Results of the Telomerization of Prenyl Chloride With Isoprene in the Presence of $ZnCl_2$ (Isoprene 78 g, prenyl chloride 120 g, catalyst $ZnCl_2$, degree of conversion 43%)

| Fraction No. | Boiling point (5 mm) | Weight (in g) | $d_4^{20}$ | $n_D^{20}$ | % Cl | Amount of | |
|---|---|---|---|---|---|---|---|
| | | | | | | geranyl chloride (in %) | dienic chlorides (in %) |
| 1 | To 65° | 1.0 | — | — | — | — | — |
| 2 | 65—75 | 3.8 | 0.9390 | 1.4742 | 14.9 | — | — |
| 3 | 75—79 | 7.8 | 0.9411 | 1.4745 | 17.6 | 21.5 | — |
| 4 | 79—82 | 18.0 | 0.9479 | 1.4756 | 19.5 | 26.5 | 35.6 |
| 5 | 82—90 | 1.0 | — | 1.4740 | — | — | — |
| 6 | 90—105 | 7.8 | 0.9447 | 1.4742 | 19.1 | — | — |
| 7 | 105—140 | 10.0 | — | 1.4872 | 12.0 | — | — |
| 8 | Residue | 20.1 | — | — | — | — | — |

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* Total chlorine by the Carius method, 20.1%.

** Total chlorine by the Carius method, 26.5%.

*** Amount of primary chlorides 37%.

*Geranyl chloride,* with b.p. 93-95° (9 mm), $d_4^{20}$ 0.9261, $n_D^{20}$ 1.4795, and a geranyl chloride content 86%, was obtained by reacting phosphorus trichloride with linalool [b.p. 82° (10 mm), $d_4^{20}$ 0.8655, $n_D^{20}$ 1.4628, $\alpha_D$ + 14.6°]. In a second experiment using the same reactants we obtained a product with b.p. 75-80° (5 mm), $d_4^{16}$ 0.9289 and $n_D^{20}$ 1.4775, with a geranyl chloride content of 65%.*

## SUMMARY

1. The telomerization of isoprene with its hydrochlorides in the presence of various catalysts was studied. It was shown that the best catalysts are stannic chloride and zinc chloride.

2. It was established that the character of the telomerization depends on the nature of the catalyst: stannic chloride favors the formation, together with geranyl chloride, of higher telomers, while zinc chloride favors the formation of terpinyl chloride.

3. It was shown that when stannic chloride and zinc chloride are used as catalysts the yield of geranyl chloride depends primarily on the degree of conversion, and with the same degree of conversion is nearly independent of the nature of the catalyst, nature of the halo derivative, temperature, or the reactant ratio, and is slightly dependent on the nature of the solvent.

4. It was shown that the composition of the mixed terpene chlorides formed in telomerization can be determined from the intensities of the frequencies of the infrared spectrum in the region of 1.6 and 10-12 μ.

## LITERATURE CITED

[1] Fr. Patent 824,909; Chem. Zentr. 1938, I, 4108.

[2] A. A. Petrov and K. V. Leets, J. Gen. Chem. 26, 1113 (1956).**

[3] K. V. Leets, Dissertation: Study of the Addition of Alkyl Halides to Compounds With a Conjugated System of Double Bonds, Lensovet Leningrad Technological Institute (1954); Author's Certificate No. 554,720 (1955).

[4] A. A. Petrov, N. A. Razumova and M. L. Genusov, J. Gen. Chem. 28, 1128 (1958).**

[5] V. N. Belov, N. A. Daev, S. D. Kustova, K. V. Leets, S. S. Poddubnaia, N. I. Skvortsova, E. I Shepelenkova and A. K. Shumeiko, J. Gen. Chem. 27, 1384 (1957).**

[6] K. V. Leets, A. K. Shumeiko, A. A. Rozenoer, N. V. Kudriashova and A. I. Piliavskaia, J. Gen. Chem. 27, 1510 (1957).*

[7] K. V. Leets, A. I. Piliavskaia and M. I. Korovkina, J. Gen. Chem. 27, 2969 (1957).**

[8] A. A. Petrov, Kh. V. Bal'ian, Iu. I. Kheruze and E. Iu. Shvarts, Author's Certificate No. 555,185 (1956).

[9] A. A. Grinberg, Introduction to the Chemistry of Complex Compounds [in Russian], p. 170 (1947).

[10] A. Laforgue, Compt. rend. 227, 352 (1948).

[11] A. A. Petrov and N. P. Sopov, J. Gen. Chem. 22, 591 (1952).**

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**See C.B. Translation.

# ACETYLENE DERIVATIVES

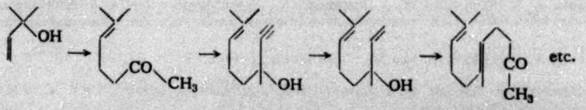
## 193. TOTAL SYNTHESIS OF ISOPRENOID ALCOHOLS (LINALOOL, GERANIOL, NEROL, NEROLIDOL, FARNESOL, GERANYLLINALOOL, GERANYLGERANIOL AND PHYTOL)

I. N. Nazarov,* B. P. Gusev and V. I. Gunar

Some 7 years ago we developed in our laboratory a simple method for the synthesis of acetylenic alcohols based on the condensation of aldehydes and ketones with acetylene under the influence of powdered potassium hydroxide and employing a slight pressure (5-10 atm) [1]. As is known, acetylenic alcohols in the presence of Pd-catalyst show quite selective hydrogenation and after the absorption of 1 mole of hydrogen are converted to the corresponding vinyl alcohols in nearly quantitative yield [2].

Earlier it had been shown [3] that tertiary vinyl alcohols when reacted with hydrogen halides are converted even in the cold almost completely into primary halo derivatives of allylic type, which are saponified with rearrangement to the original tertiary vinyl alcohols, and when reacted with salts of acids, followed by saponification, give primary alcohols of allylic type.

In view of the fact that dimethylvinylcarbinol has become a readily available technical product at the present time, we decided to make a detailed study of methods for the total synthesis of natural isoprenoid alcohols based on it (and also based on isoprene), employing for this purpose the multiple repetition of the following cycle of reactions:



Consequently, with such a scheme the isoprenoid chain is built by a successive coupling of the reactions of ethynylation, selective hydrogenation, isomerization and acetonylation, in which connection the last two reactions are usually run in one step without isolating the intermediate products. We made a detailed study of the entire path of this synthesis up to the isoprenoid alcohols $C_{20}$ (geranylgeraniol and phytol), the results of which are represented by the schemes shown on the next page.

In all cases the condensation of ketones (II, VI, X, XIV, XVIII, XXII) with acetylene was run by the earlier developed method [1] in the presence of powdered potassium hydroxide under an acetylene pressure of 5-10 atm, and here the tertiary acetylenic alcohols (III, VII, XI, XV, XIX, XXIII) were obtained in 87-93% yield. In the presence of palladium on calcium carbonate the obtained acetylenic alcohols smoothly underwent selective hydrogenation (1 mole of hydrogen) to yield the corresponding tertiary vinyl alcohols (IV, VIII, XII, XVI, XX, XXIV) in 90-96% yield. The tertiary vinyl alcohols were then converted to the unsaturated ketones (II), (VI), (X), (XVII) and (XXI) (acetonylation reaction) by three different methods, all of which had recently been studied in detail in our laboratory [19].

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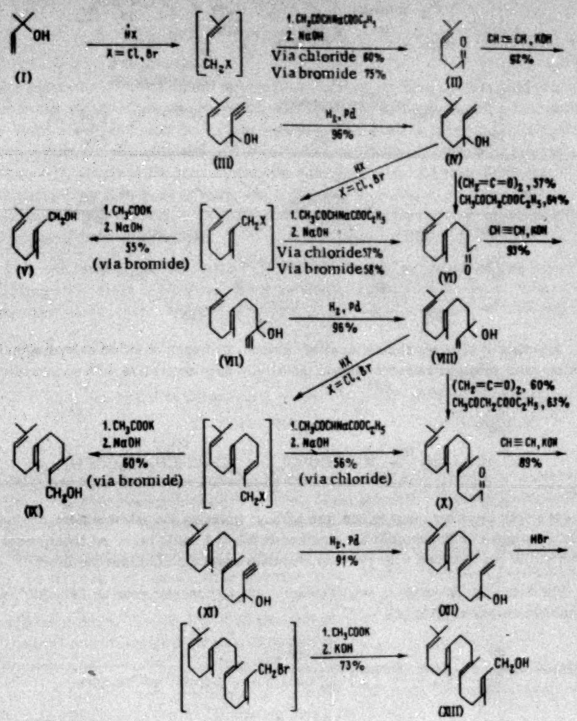
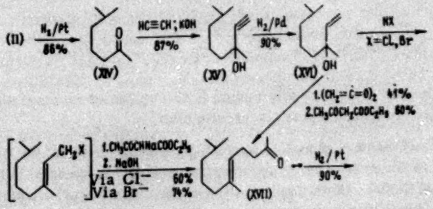
* Deceased.

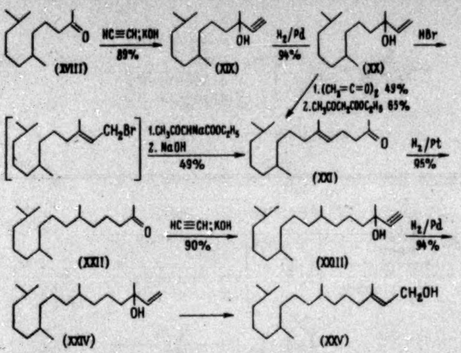
**Synthesis of Geraniol (V), Farnesol (IX) and Geranylgeraniol (XIII)**


(I)
HX
X = Cl, Br
1. CH3COCHNaCOOC2H5
2. NaOH
Via chloride 60%
Via bromide 75%
(II)
CH≡CH, KOH
62%
(III)
H2, Pd
96%
(IV)
HX
X = Cl, Br
(CH2=C=O)2, 37%
CH3COCH2COOC2H5, 64%
1. CH3COOK
2. NaOH
55%
(via bromide)
(V)
1. CH3COCHNaCOOC2H5
2. NaOH
Via chloride 57%
Via bromide 58%
(VI)
CH≡CH, KOH
93%
(VII)
H2, Pd
96%
(VIII)
HX
X = Cl, Br
(CH2=C=O)2, 60%
CH3COCH2COOC2H5, 63%
1. CH3COOK
2. NaOH
60%
(via bromide)
(IX)
1. CH3COCHNaCOOC2H5
2. NaOH
56%
(via chloride)
(X)
CH≡CH, KOH
89%
(XI)
H2, Pd
91%
(XII)
HBr
1. CH3COOK
2. KOH
73%
(XIII)

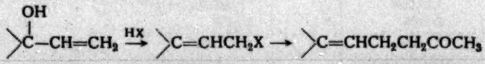
**Synthesis of Phytol (XXV)**


(II)
H2/Pt
86%
(XIV)
HC≡CH; KOH
87%
(XV)
H2/Pd
90%
(XVI)
HX
X = Cl, Br
1. (CH2=C=O)2 41%
2. CH3COCH2COOC2H5 60%
1. CH3COCHNaCOOC2H5
2. NaOH
Via Cl⁻ 60%
Via Br⁻ 74%
(XVII)
H2/Pt
90%

(continued on next page)



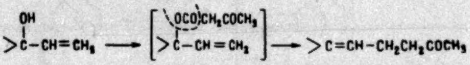
Method A. Reaction of vinyl alcohols with either gaseous hydrogen chloride or hydrogen bromide (usually in isooctane solution), with subsequent condensation of the allylic halo derivative with sodioacetoacetic ester, and saponification.



$$>\overset{OH}{\underset{|}{C}}-CH=CH_2 \xrightarrow{HX} >C=CHCH_2X \rightarrow >C=CHCH_2CH_2COCH_3$$

It is expedient to run these reactions in one step without isolating the intermediate products, and here the unsaturated ketones (analogs of allylacetone) are obtained in 50-75% yield based on taken vinyl alcohol. Usually somewhat higher yields are obtained with the bromides than when the chlorides are used.

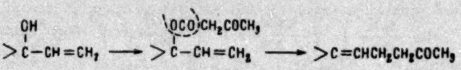
Method B. Direct reaction of tertiary vinyl alcohols with acetoacetic ester at 140-200°, with simultaneous cleavage of alcohol and carbon dioxide [4].



$$>\overset{OH}{\underset{|}{C}}-CH=CH_2 \longrightarrow \left[>\overset{OCOCH_2COCH_3}{\underset{|}{C}}-CH=CH_2\right] \longrightarrow >C=CH-CH_2CH_2COCH_3$$

With this method the unsaturated ketones (II), (VI), (X), (XVII) and (XXI) are obtained in 60-65% yield (based on vinyl alcohol), and this method is most suitable for operating on a larger scale.

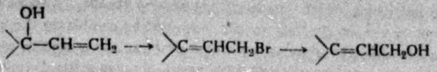
Method C. Reaction of tertiary vinyl alcohols with diketene (in the presence of pyridine or triethylamine), followed by pyrolysis of the acetoacetic ester, obtained here in about 90% yield, at 170-200° [5].



$$>\overset{OH}{\underset{|}{C}}-CH=CH_2 \longrightarrow >\overset{OCOCH_2COCH_3}{\underset{|}{C}}-CH=CH_2 \longrightarrow >C=CHCH_2CH_2COCH_3$$

The yield of unsaturated ketones by this method is 40-60% (based on vinyl alcohol), and the reaction can be run in one step without isolating the pure acetoacetic ester.

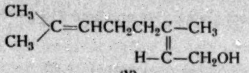
We also made a detailed study of various methods for the conversion of the tertiary vinyl alcohols (IV), (VIII), (XII) and (XXIV) to the corresponding terpene primary alcohols–geraniol (V), farnesol (IX), geranylgeraniol (XIII) and phytol (XXV). Direct isomerization of the tertiary vinyl alcohols using sulfuric acid [6] proved to be completely unsuitable in the present case. Reaction of the tertiary vinyl alcohols with acetic anhydride in the presence of acids, followed by saponification, also did not give very satisfactory results. The best results were obtained by reacting the tertiary vinyl alcohols with either gaseous hydrogen bromide on hydrogen chloride (in isooctane solution), followed by reaction of the allylic bromides with potassium acetate in dimethylformamide solution, and then saponification of the formed acetates with 10% caustic.



$$\overset{OH}{\overset{|}{>C}}-CH{=}CH_2 \longrightarrow >C{=}CHCH_2Br \longrightarrow >C{=}CHCH_2OH$$

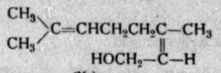
All of these reactions were run in one step without isolating the intermediate products, which made it possible to increase the yields of primary terpene alcohols substantially and simplify their method of preparation. The reaction of the allylic halo derivatives with potassium acetate is best run in dimethylformamide solution. Satisfactory results are also obtained in alcohol solutions (methanol, ethanol); however, here the corresponding ethers (methyl, ethyl) of the primary terpene alcohols are formed as by-products. Other solvents (dioxane, acetone) give poorer results, apparently due to the poor solubility of potassium acetate in them. The use in this reaction of sodium acetate, or of the sodium and potassium salts of other acids (formic, butyric, benzoic), also does not give good results.

With the above-described method linalool (IV) is isomerized to a mixture of geraniol (V) and nerol (Va) in the ratio 5: 3, in a total yield of 55-60%. These geometric isomers can be easily separated by chromatographing on aluminum oxide; here the nerol is completely eluted with petroleum ether, and the geraniol with methanol.



$$\begin{matrix}CH_3\diagdown\\ \phantom{CH_3}C{=}CHCH_2CH_2C{-}CH_3\\ CH_3\diagup\end{matrix}\qquad\begin{matrix}\Vert\\ H{-}C{-}CH_2OH\end{matrix}$$

(V)



$$\begin{matrix}CH_3\diagdown\\ \phantom{CH_3}C{=}CHCH_2CH_2C{-}CH_3\\ CH_3\diagup\end{matrix}\qquad\begin{matrix}\Vert\\ HOCH_2{-}C{-}H\end{matrix}$$

(Va)

Consequently, we were the first to accomplish the total synthesis of nerol, extremely important in perfumery and a very difficultly available terpene alcohol found in small amounts together with geraniol in certain valuable essential oils (rose oil, bergamot oil, tuberose oil, etc.).

With the same method nerolidol (VIII) is converted in 60% yield to farnesol, formed only as the isomer corresponding to the natural compound. As is known, it is very difficult to obtain farnesol from natural sources. It is the odor principle found in linden blossoms, and in the seeds of the musk and some other plants, containing it in small concentrations. Farnesol is of interest not only for perfumery, but also for the further synthesis of a number of natural and biologically active compounds.

The conversion of geranyllinalool (XII) to geranylgeraniol (XIII) goes even more smoothly; here, the same as in the case of farnesol, only one isomer is formed in 73% yield, The same method was also used to synthesize isophytol (XXIV), as shown in the scheme given previously.

Phytol is one of the more important natural alcohols. As is known, it is found in chlorophyll, which at the present time serves as the only natural source for obtaining it. The practical importance of phytol, and also of geranylgeraniol and the alcohols (XXIV) and (XII) isomeric with it, is associated primarily with the synthesis of vitamins K and E (tocopherol) and other biologically important compounds.

The availability of the starting products, simplicity of the operations, and the high yields at all stages, make the above described synthesis entirely suitable for the commercial preparation of isoprenoid alcohols (linalool, geraniol, nerol, nerolidol, farnesol, geranyllinalool, geranylgeraniol and phytol), representing great interest for perfumery and the synthesis of some important natural compounds (vitamins A, E and K, carotenoids, terpenes, etc.).

The above scheme for the synthesis of isoprenoid alcohols also repeatedly attracted the attention of earlier investigators [7-11]. However, up to now this scheme remained quite undeveloped and was completely unsuitable for the large-scale production of isoprenoid alcohols, since all three repeating steps of this synthesis (ethynylation, acetonylation and isomerization of tertiary vinyl alcohols to primary terpene alcohols) were in their methods either unsuitable for large-scale operation or gave low yields.

In particular, the major difficulties were encountered in the condensation of acetylene with unsaturated ketones (of the allylacetone type), which was usually run in liquid ammonia solution, gave quite low yields of the corresponding acetylenic alcohols, was difficult to run, and was unsuitable for operating with large quantities of material. The main drawbacks encountered in the isomerization of tertiary vinyl alcohols to primary terpene alcohols were the low yields, which usually did not exceed 20-30%. A basic improvement in all of the schemes for the synthesis of isoprenoid alcohols was also achieved by combining the above mentioned isomerization of tertiary vinyl alcohols with acetonylation, running the two as one operation with the yield of unsaturated ketones–analogs of allylacetone–being equal to 60-75%, based on taken tertiary vinyl alcohol.

## EXPERIMENTAL

Preparation of methylheptenone (II). a) A stream of 193 g (2.4% excess)of hydrogen bromide was passed in 3 hours into 200 g of dimethylvinylcarbinol (I) with ice-water cooling. After holding at room temperature for 90 minutes the aqueous layer (40 ml) was separated, the bromide washed with saturated sodium bicarbonate solution, then with water, and finally dried over magnesium sulfate. We obtained 323 g of crude bromide, which without further purification was added in an hour at 0-5° to a solution of sodioacetoacetic ester, prepared from 55 g of sodium metal and 380 g of acetoacetic ester in 650 ml of anhydrous alcohol. The reaction mixture was stirred for 3 hours at room temperature and for 4 hours at 60°, after which the precipitate of sodium bromide (213 g) was filtered, the alcohol distilled under slight vacuum, and the residue treated with 1 liter of 10% sodium hydroxide solution. The mixture was stirred vigorously for 2 hours at room temperature and for 3 hours at 60-65°, cooled, acidified with concentrated hydrochloric acid (to Congo), the methylheptenone extracted with ether, the ether extract washed with saturated sodium bicarbonate solution, then with water, and finally dried over magnesium sulfate. After removal of the ether by distillation the residue was first vacuum-distilled and then through a column with an efficiency of 25 theoretical plates. We obtained 219 g (75%, based on dimethylvinylcarbinol) of methylheptenone,.

B.p. 75.5-76° (25 mm), $n_D^{20}$ 1.4404, $d_4^{20}$ 0.8615, MR 38.89; calculated 38.69.

The semicarbazone had m.p. 135.5-136° (from 80% ethanol)[12].

b) A stream of 39.5 g (8% excess) of hydrogen chloride was passed in 4 hours into 86 g of dimethylvinylcarbinol with ice-water cooling. After holding at room temperature for 2 hours the aqueous layer (20 ml) was separated, the chloride washed with saturated bicarbonate solution, and then dried over magnesium sulfate. The chloride without further purification was used in the reactions with sodioacetoacetic ester.

The above-described chloride was added in 90 minutes to a solution of sodioacetoacetic ester prepared from 34 g of sodium metal and 190 ml of acetoacetic ester in 300 ml of methanol. The temperature of the reaction mass was 30-40°. The mixture was stirred at this temperature for another 2 hours, after which the methanol was distilled off, and the residue was treated with 600 ml of 10% sodium hydroxide solution. After stirring at 60-70° for 3 hours the reaction mixture was cooled, acidified with concentrated hydrochloric acid (to Congo), the methylheptenone layer was separated, the aqueous layer was extracted 4 times with ether, the combined ether solution was washed with saturated sodium bicarbonate solution, then with water, and finally dried over magnesium sulfate. After removal of the ether by distillation the residue was vacuum-distilled. We obtained 76.3 g (60%) of methylheptenone with b.p. 54-56° (9 mm); $n_D^{21}$ 1.4397.

The semicarbazone had m.p. 135-136°.

The preparation of methylheptenone by methods B and C had been described by us earlier [19].

Preparation of dehydrolinalool (III). Into a 6-liter steel reactor [1] was charged 3.5 liters of absolute ether, 360 g of powdered potassium hydroxide and 20 ml of ethanol. After blowing with nitrogen the reaction mass was saturated with acetylene to a pressure of 6 atm, and then 680 g of methylheptenone was added from a steel dropping funnel under pressure in 1.5 hours at 2-4°. The reaction mass was stirred under an acetylene pressure of 6-7 atm for 2 hours at 4-5° and for 2 hours at room temperature. Then the excess acetylene was removed and 720 ml of water was added, the mixture stirred vigorously for 15 minutes, the ether layer separated, the aqueous layer extracted with ether, and the combined ether solution neutralized with carbon dioxide and dried over magnesium sulfate. The ether was removed by distillation and the residue was vacuum-distilled. We obtained 750 g (92%) of dehydrolinalool.

B.p. 82-83° (10 mm), $n_D^{20}$ 1.4632, $d_4^{20}$ 0.8788 [13], MR 47.44; calculated 47.63.

Preparation of linalool (IV). Into a 3-liter steel reactor, fitted with stirrer and water jacket for cooling, was charged 740 g of dehydrolinalool and 1.2 g of palladium catalyst, deposited on calcium carbonate. The hydrogenation was run at 12-15° (with cooling) and a hydrogen pressure of 2-3 atm. The amount of hydrogen absorbed in 2.5 hours was 110 liters, after which the test for acetylenic hydrogen showed negative. (The sensitivity of the acetylenic test using an ammoniacal solution of silver nitrate in alcohol is 0.3-0.5%). We obtained 723 g (96%) of linalool.

B.p. 80-82° (10 mm) [13], $n_D^{20}$ 1.4622, $d_4^{20}$ 0.8664, MR 48. 96; calculated 48.97.

Found %: C 77.59, 77.64; H 11.87, 11.86. $C_{10}H_{18}O$. Calculated %: C 77.87; H 11.80.

By means of special experiments it was established that the degree of selectivity shown by dimethylethynylcarbinol when hydrogenated with Pd-catalyst on calcium carbonate is not less than 99.5%. Other acetylenic alcohols, containing unsubstituted acetylenic hydrogen, also hydrogenate in a similar manner. Platinum and nickel catalysts lack the ability of promoting the selective hydrogenation of acetylenic alcohols and cannot be used in these reactions to obtain pure vinyl alcohols. All of the other acetylenic alcohols were hydrogenated in the same manner as described above; large quantities (over 200 g) were hydrogenated in a steel reactor under pressure, while small amounts (under 200 g) were hydrogenated in a glass bottle at atmospheric pressure. The palladium catalyst, deposited on calcium carbonate, was prepared in conventional manner [14], and contained about 5% palladium.

Isomerization of linalool to geraniol (V) and nerol (Va). A stream of 85 g (5% excess) of hydrogen bromide was passed in 1 hour into 154 g of linalool at 5°. After holding at room temperature for 2 hours the aqueous layer (18 ml) was separated, the bromide washed quickly with cold saturated bicarbonate solution, then with water, and finally dried over magnesium sulfate. We obtained 184 g of crude bromide, which was added in 15 minutes at room temperature to a solution of 98 g of potassium acetate in 700 ml of dimethylformamide (the potassium acetate dissolved only partially). Then the mixture was stirred for 2 hours at room temperature and for 2 hours at 45-50°. The precipitate of potassium bromide (112 g) was filtered, while the dimethylformamide was vacuum-distilled at 20 mm. The residue was treated with 800 ml of 10% sodium hydroxide solution and the mixture stirred for 4 hours at 70°. The product was extracted with ether and dried over magnesium sulfate. The ether was removed by distillation and the residue was vacuum-distilled. We obtained 92 g of mixed geraniol and nerol with b.p. 103-110° (9 mm), $n_D^{20}$ 1.4754, which was easily separated by chromatographing through a column containing aluminum oxide (activity II, diameter of column 32 mm, height 700 mm). Elution with 1 liter of petroleum ether enabled us to isolate 31.2 g (20%, based on linalool) of nerol.

B.p. 103-105° (9 mm), $n_D^{20}$ 1.4744, $d_4^{20}$ 0.8762, MR 49.50; calculated 48.96.

Calculated %: C 77.93, 77.77; H 11.80, 11.71. $C_{10}H_{18}O$. Calculated %: C 77.87; H 11.68

The diphenylurethan had m.p. 50.5-51° [15].

Elution with 500 ml of methanol gave us 53.8 g (35%, based on linalool) of geraniol.

B.p. 109-100° (9 mm), $n_D^{20}$ 1.4760, $d_4^{20}$ 0.8806, MR 49.39; calculated 48.96.

Found %: C 77.60, 77.52; H 11.76, 11.72. $C_{10}H_{18}O$. Calculated %: C 77.87; H 11.68.

The diphenylurethan had m.p. 81-81.5° [16].

Preparation of geranylacetone (VI). Method A. a) A stream of 165 g (1.8% excess) of hydrogen bromide was passed in 2 hours into 308 g of linalool with ice-water cooling. After holding at room temperature for 2 hours the aqueous layer (35 ml) was separated, the bromide washed quickly with saturated bicarbonate solution, then with water, and finally dried over magnesium sulfate. We obtained 418 g of crude bromide, which was added in 1 hour at 2-5° to a solution of sodioacetoacetic ester, prepared from 46 g of sodium metal and 280 g of acetoacetic ester in 600 ml of anhydrous alcohol. The reaction mass was stirred for 2 hours at 2-5°, then 3 hours at room temperature, and finally 3 hours at 60-65° with simultaneous removal of the alcohol by distillation under slight vacuum. The residue was treated with 1 liter of 10% sodium hydroxide solution and the mixture stirred for 3 hours at 60-65°. Then the mixture was cooled and acidified with concentrated hydrochloric acid (to Congo), the product extracted with ether, and the ether extract washed with bicarbonate solution, then with water, and dried over magnesium sulfate. After removal of the ether by distillation we obtained 226 g of geranylacetone (58%, based on linalool).

B.p. 133-135° (20 mm), $n_D^{20}$ 1.4664, $d_4^{20}$ 0.8696, MR 61.93; calculated. 61.34.

Found %: C 80.05, 80.07; H 11.35, 11.50. $C_{13}H_{22}O$. Calculated %: C 80.34; H 11.41.

The semicarbazone had m.p. 93-94° (from 60% ethanol) [8].

b) A stream of 38.5 g (5.5% excess) of hydrogen chloride was passed in 1 hour with ice-water cooling into 154 g of linalool. After holding at room temperature for 3 hours the aqueous layer (18 ml) was separated, and the chloride was washed quickly with bicarbonate solution, then with water, and dried over magnesium sulfate. We obtained 158 g of crude chloride, which was added in 40 minutes at 5-7° to a solution of sodioacetoacetic ester, prepared from 23 g of sodium metal and 140 g of acetoacetic ester in 300 ml of anhydrous alcohol The reaction mass was stirred for 2 hours at 5-7°, then for 4 hours at room temperature, and finally for 3 hours at 60-65° with simultaneous removal of the alcohol by distillation under slight vacuum. The residue was treated with 500 ml of 10% sodium hydroxide solution, the mixture stirred for 3 hours at 60-65°, and then worked up in the same manner as described above.

We obtained 111 g (57%, based on linalool) of geranylacetone with b.p. 132-134° (19 mm), $n_D^{20}$ 1.4664.

Method B. A mixture of 462 g of linalool and 1170 g of acetoacetic ester was heated for 3 hours at 120-198°. Here 170 ml of liquid with b.p. 60-82° distilled and 57 liters (84.5%) of carbon dioxide was evolved. After removal of the excess acetoacetic ester (720 g) by distillation the residue was washed with bicarbonate solution, then with water, and finally dried over magnesium sulfate. Fractional distillation in vacuo gave 375 g (64.5%) of geranylacetone with b.p. 120-122° (10 mm), $n_D^{20}$ 1.4666. Carroll, the first to run this reaction (in the presence of sodium ethylate), obtained a 41% yield of geranylacetone [4].

Method C. One gram of anhydrous pyridine and 35 g of diketene were added in 20 minutes to 54 g of linalool with stirring and water cooling. The mixture was stirred for 3 hours at room temperature, 2 hours at 70°, and then it was heated for 30 minutes at 140-195°. Here 6.1 liters (78%) of carbon dioxide was liberated. The residue was washed with bicarbonate solution, then with water, and finally dried over magnesium sulfate. Fractional distillation gave 38.5 g (56.5%) of geranylacetone with b.p. 133-135° (20 mm), $n_D^{20}$ 1.4666. This reaction was first run by Kimel and Cope [5], who obtained a 47.5% yield of geranylacetone in this manner.

Preparation of dehydronerolidol (VII). A mixture of 2.5 liters of ether and 112 g of potassium hydroxide was charged into a steel reactor, acetylene was introduced to a pressure of 7 atm, and then 320 g of geranylacetone was added in 1 hour at 0°. The reaction mass was stirred at 0.5° for 2 hours and at room temperature for 3 hours. Then 250 ml of water was added, the mixture stirred for 15 minutes, and the product worked up in the same manner as described above for the synthesis of dehydrolinalool. We obtained 338 g (93%) of dehydronerolidol [17].

B.p. 117-119° (0.6 mm), $n_D^{20}$ 1.4798, $d_4^{20}$ 0.8886, MR 70.31; calculated 70.06.

Found %: C 81.60 81.70; H 10.94, 11.10. $C_{15}H_{20}O$. Calculated %: C 81.81. H 10.91.

Preparation of nerolidol (VIII). For this 130 g of dehydronerolidol was hydrogenated in the presence of 0.25 g of palladium catalyst, deposited on calcium carbonate. In 3 hours 14.05 liters (17°, 746 mm) of hydrogen was absorbed and the acetylenic bond had disappeared. We obtained 126.1 g (96.4%) of nerolidol [17].

B.p. 94° (0.18 mm), $n_D^{20}$ 1.4784, $d_4^{20}$ 0.8752, MR 71.86; calculated 71.60

Found %: C 80.88, 80.80; H 11.79, 11.83. $C_{15}H_{26}O$. Calculated %: C 81.08, H 11.71.

Isomerization of nerolidol to farnesol (IX). A stream of 43 g (6% excess) of gaseous hydrogen bromide was passed in 1 hour with ice-water cooling into a mixture of 111 g of nerolidol and 100 ml of isooctane. After holding at room temperature for 2 hours the aqueous layer (9 ml) was separated, the bromide washed quickly with cold bicarbonate solution, then with water, dried over magnesium sulfate, and the isooctane vacuum-distilled. We obtained 138 g of crude bromide, which was added in 30 minutes at room temperature to a solution of 50 g of potassium acetate in 500 ml of dimethylformamide (the potassium acetate failed to dissolve completely). The mixture was stirred at room temperature for 3 hours and at 55-60° for 2 hours. The precipitate of potassium bromide (60 g) was filtered, the dimethylformamide was vacuum-distilled, and the residue was treated with 300 ml of 10% potassium hydroxide solution.

The mixture was stirred for 4 hours at 65-70°, and the product was worked up in the same manner as described above in the experiment on the isomerization of linalool. We obtained 70 g of farnesol with b.p. 108-112° (0.18 mm), $n_D^{20}$ 1.4868. After purification by chromatographing on aluminum oxide we obtained 67 g of pure farnesol [18] (60%, based on nerolidol).

B.p. 126-127° (0.5 mm), $n_D^{20}$ 1.4872, $d_4^{20}$ 0.8886, MR 72.02; calculated 71.60.

Found %: C 81.14, 81.27; H 11.69, 11.56. $C_{15}H_{26}O$. Calculated %: C 81.08; H 11.71.

Preparation of farnesylacetone (X). Method A. a) Four grams (11% excess) of hydrogen chloride was passed in 30 minutes with ice-water cooling into a solution of 22.2 g of nerolidol in 20 ml of isooctane. After holding at room temperature for 2 hours the aqueous layer (1.6 ml) was separated, the chloride washed quickly with bicarbonate solution, then with water dried over magnesium sulfate, and the isooctane vacuum-distilled. The crude chloride was then added in 20 minutes at 5-7° to a solution of sodioacetoacetic ester, prepared from 2.3 g of sodium metal and 14 g of acetoacetic ester in 100 ml of anhydrous methanol. The mixture was stirred for 3 hours at room temperature and for 2 hours at 60° with simultaneous removal of the methanol by distillation under slight vacuum. The residue was treated with 70 ml of 10% potassium hydroxide solution, the mixture stirred for 2 hours at room temperature, then for 2 hours at 50-55°, and finally it was worked up in the usual manner. We obtained 14.6 g of farnesylacetone [7] (55.7%, based on nerolidol).

B.p. 143-144° (0.42 mm), $n_D^{20}$ 1.4810, $d_4^{20}$ 0.8904, MR 83.87; calculated 83.93.

Found %: C 82.27, 82.40; H 11.58, 11.56. $C_{18}H_{30}O$. Calculated %: C 82.38; H 11.52.

The semicarbazone had m.p. 81.5-82° (from 60% ethanol) [9].

Method B. A mixture of 55 g of nerolidol and 98 g of acetoacetic ester was heated for 2 hours at 140-190°. Here 22 ml of liquid with b.p. 60-76° distilled and 4.8 liters (84%) of carbon dioxide was evolved. After removal of the excess acetoacetic ester by distillation the residue was washed with bicarbonate solution, then with water, and dried over magnesium sulfate. We obtained 41.6 g (63%) of farnesylacetone with b.p. 156-158° (1 mm), $n_D^{20}$ 1.4814.

Method C. A mixture of 22.2 g of nerolidol, 9.5 g of diketene and 0.5 g of pyridine was stirred for 3 hours at room temperature, for 2 hours at 60°, and then heated for 30 minutes at 140-195°. Here 1.64 liters (72.5%) of carbon dioxide was evolved. The residue was treated with bicarbonate solution, then with water, and dried over magnesium sulfate. We obtained 15.8 g (60%) of farnesylacetone with b.p. 120-123° (0.18 mm), $n_D^{20}$ 1.4808.

Preparation of geranyldehydrolinalool (XI). A mixture of 1 liter of absolute ether, 25 g of powdered potassium hydroxide and 10 ml of ethanol was charged into a steel reactor. Then 60 g of farnesylacetone was added in 30 minutes at 0° and an acetylene pressure of 9 atm. The mixture was stirred at room temperature for 5 hours, the acetylene vented, 50 ml of water added, the mixture stirred for 15 minutes, and the product worked up in the usual manner. We obtained 58.5 g (89%) of geranyldehydrolinalool [7].

B.p. 144-145° (0.3 mm), $n_D^{20}$ 1.4892, $d_4^{20}$ 0.8952, MR 93.07; calculated, 92.68.

Found %: C 83.23, 83.41; H 11.14, 11.24. $C_{20}H_{32}O$. Calculated %: C 83.27; H 11.18.

Preparation of geranyllinalool (XII). A solution of 55 g of geranyldehydrolinalool in 100 ml of methanol was hydrogenated in the presence of Pd-catalyst. In 2 hours 4.5 liters (20°, 748 mm) of hydrogen was absorbed and the test for acetylenic hydrogen became negative. We obtained 50.2 g (91%) of geranyllinalool [7].

B.p. 144-146° (0.32 mm), $n_D^{20}$ 1.4874, $d_4^{20}$ 0.8852, MR 94.39; calculated 94.21.

Found %: C 82.33, 82.00; H 12.07, 12.04. $C_{20}H_{34}O$. Calculated %: C 82.69; H 11.80.

Isomerization of geranyllinalool to geranylgeraniol (XIII). Six grams (7% excess) of hydrogen bromide was passed in 30 minutes with ice-water cooling into a solution of 20 g of geranyllinalool in 50 ml of isooctane. After holding at room temperature for 2 hours the aqueous layer (1.2 ml) was separated, the bromide washed quickly with cold bicarbonate solution, then with water, dried over magnesium sulfate, and the isooctane vacuum-distilled. The obtained bromide was added in 10 minutes to a solution of 7 g of potassium acetate in 150 ml of dimethylformamide. The mixture was stirred for 3 hours at room temperature and for 2 hours at 60-65°. The precipitate of potassium bromide (8.5 g) was filtered, the dimethylformamide was vacuum-distilled, and the residue was treated with 60 ml of 10% potassium hydroxide solution. The mixture was stirred for 4 hours at 60-65° and the product was worked up in the usual manner. We obtained 16.1 g of geranylgeraniol with b.p. 160-165° (0.32 mm), which after purification by chromatographing on aluminum oxide gave 14.6 g (73%) of pure geranylgeraniol [7].

B.P. 162-164° (0.32 mm), $n_D^{20}$ 1.4948, $d_4^{20}$ 0.8922, MR 94.75; calculated 94.21.

Found %: C 82.60, 82.38; H 11.87, 11.91. $C_{20}H_{34}O$. Calculated %: C 82.69; H 11.80.

Preparation of methylheptanone (XIV). a) To a solution of sodioacetoacetic ester, obtained from 85 g of sodium metal and 470 ml of acetoacetic ester in 1000 ml of methanol, was added 646 g of isoamyl iodide. The mixture was stirred for 4 hours at room temperature and for 5 hours at 64°. The methanol was distilled off and the residue was saponified with 15% sodium hydroxide solution at the boil for 6 hours. Then the mixture was cooled and acidified with concentrated hydrochloric acid, after which the product was extracted with ether, washed with saturated bicarbonate solution, then with water, and dried over calcium chloride. The ether was distilled off and the residue was vacuum-distilled to give 240 g (47%) of methylheptanone with b.p. 41-42° (6 mm), $n_D^{20}$ 1.4135.

b) The hydrogenation of 696 g of methylheptenone (II) was run in a steel autoclave at room temperature in the presence of 1.5 g of platinum oxide and a hydrogen pressure of 100-20 atm. In 6 hours the hydrogen absorption was 140 liters (theory is 134 liters of hydrogen). The test with tetranitromethane did not give a yellow color. The catalyst was filtered and the residue was vacuum-distilled. We obtained 600 g (86%) of methylheptanone with b.p. 46.5-48° (7 mm), $n_D^{20}$ 1.4144.

The semicarbazone had m.p. 154-155° (from aqueous methanol) [20].

Preparation of 3,7-dimethyl-1-octyn-3-ol (XV). A mixture of 3.5 liters of absolute ether, 400 g of powdered potassium hydroxide and 20 ml of ethanol was charged into a 6-liter steel autoclave. After purging the system with nitrogen the reaction mass was saturated with acetylene to a pressure of 7 atm, and then 500 g of methylheptanol was added in 1 hour at 8-10°. The reaction mass was stirred for another 3 hours, the excess acetylene removed, 800 ml of water added, and after stirring for 15 minutes the product was worked up in the usual manner. We obtained 524 g (87%) of 3,7-dimethyl-1-octyn-3-ol with b.p. 69-71° (7 mm), $n_D^{20}$ 1.4398.

Found %: C 77.46, 77.45; H 11.64, 11.63. $C_{10}H_{18}O$. Calculated %: C 77.88; H 11.73.

3,5-Dinitrobenzoate, m.p. 79.5-80.5°.

Found %: N 8.33, 8.61. $C_{17}H_{20}O_6N_2$. Calculated %: N 8.05.

Preparation of 3,7-dimethyl-1-octen-3-ol (dihydrolinalool) (XVI). The hydrogenation of 246 g of 3,7-dimethyl-1-octyn-3-ol at atmospheric pressure in the presence of Pd-catalyst on calcium carbonate (5% palladium content) until 38.5 liters of hydrogen was absorbed required 4 hours. Theory for hydrogen absorption is 38.6 liters. The end of hydrogenation was determined by the acetylenic test with ammoniacal silver nitrate solution. The catalyst was filtered, and the product was vacuum-distilled. We obtained 222 g (90%) of 3,7-dimethyl-1-octen-3-ol [21] with b.p. 68-70 (6 mm), $n_D^{20}$ 1.4390.

Found %: C 76.35, 76.55; H 13.32, 13.14. $C_{10}H_{20}O$. Calculated %: C 76.65; H 12.90.

Preparation of 3,7-dimethyl-3-octanol (tetrahydrolinalool). A solution of 26.4 g of 3,7-dimethyl-1-octen-3-ol in methanol was hydrogenated over platinum oxide at atmospheric pressure. Here 3.9 liters of hydrogen was absorbed. The calculated amount of hydrogen is 4.15 liters. The catalyst was filtered, and the filtrate was fractionally distilled in vacuo. We obtained 25.5 g of 3,7-dimethyl-3-octanol.

B.p. 71-73° (6mm), $n_D^{20}$ 1.4331, $d_4^{20}$ 0.8294, MR 49.62; calculated 49.90.

The 3,5-dinitrobenzoate had m.p. 45.5-46.5°.

Found %: C 57.86, 58.02; H 6.96, 6.94; N 8.02, 8.07. $C_{17}H_{24}O_6N_2$. Calculated %: C 58.01; H 6.87; N 7.95.

Preparation of 6,10-dimethyl-5-undecen-2-one (tetrahydropseudoionone) (XVII). Method A. a) A stream of 3.8 g (5% excess) of hydrogen chloride was passed with ice-water cooling into a solution of 15.6 g of 3,7-

-dimethyl-1-octen-3-ol in 25 ml of isooctane. After holding at room temperature for 2 hours the aqueous layer (1.7 ml) was separated, the chloride washed with saturated sodium bicarbonate solution, then with water, and dried over magnesium sulfate.

Without further purification the obtained chloride was added in 20 minutes at −13° to a solution of sodioacetoacetic ester, obtained from 2.4 g of sodium metal and 14 ml of acetoacetic ester in 50 ml of methanol. The mixture was stirred for 2 hours at from −13° to 0°, then for 2 hours at 18°, and the next day for another 5 hours at 50°. A solution of 7 g of sodium hydroxide in 60 ml of water was then added to the reaction mass and the whole stirred for 5 hours at 60-65°. The mixture after cooling was acidified with concentrated hydrochloric acid, the product extracted with ether, and the ether extract washed with saturated bicarbonate solution, then with water, and dried over magnesium sulfate. After removal of the ether by distillation and vacuum-distillation of the residue we obtained 11.8 g (60%) of tetrahydropseudoionone with b.p. 83-85° (2 mm), $n_D^{20}$ 1.4472.

b) A stream of 144 g (6% excess) of hydrogen bromide was passed with ice-salt cooling into a solution of 257 g of 3,7-dimethyl-1-octen-3-ol in 100 ml of isooctane. After holding for 5 hours at room temperature the aqueous layer (32 ml) was separated, the bromide washed with saturated bicarbonate solution, then with water, and dried over magnesium sulfate.

Without further purification the obtained bromide was added in two hours to a −13° solution of sodioacetoacetic ester, obtained from 40 g of sodium metal and 240 ml of acetoacetic ester in 600 ml of methanol. The mixture was then stirred for 5 hours at from −13 to + 18° and allowed to stand overnight. The next day the mixture was stirred for another 5 hours at 60°, 2/3 of the methanol was distilled under slight vacuum, and the residue was saponified with a solution of 120 g of sodium hydroxide in 900 ml of water for 5 hours at 70° After cooling, the product was acidified with concentrated hydrochloric acid and worked up in the usual manner.

We obtained 239 g (74%) of tetrahydropseudoionone with b.p. 75-77° (1 mm), $n_D^{18}$ 1.4498.

Method B. A mixture of 184.7 g of 3,7-dimethyl-1-octen-3-ol and 450 ml of acetoacetic ester was heated for 1 hour at 160-210°. Here 16 liters (68%) of carbon dioxide was evolved. The excess acetoacetic ester was distilled off, and the residue was washed 3 times with 10% sodium bicarbonate solution, then with water, and dried over magnesium sulfate. Fractional distillation in vacuo gave 129.0 g (60%) of tetrahydropseudoionone with b.p. 84-85° (1 mm), $n_D^{20}$ 1.4481.

Found %: C 79.10, 79.00; H 12.30, 12.20. $C_{13}H_{24}O$. Calculated %: C 79.52; H 12.32.

Both the semicarbazone and the 2,4-dinitrophenylhydrazone melted at room temperature.

Method C. Diketene (17.5 g) and 10 drops of anhydrous pyridine were added to 23.4 g of 3,7-dimethyl-1-octen-3-ol. The temperature of the reaction mixture rose from 20 to 36°. The mixture was stirred for 7 hours, allowed to stand overnight, then stirred for another hour at 60-80°, cooled, washed with 10% sodium bicarbonate solution, then with water, and dried over magnesium sulfate. Fractional distillation in vacuo gave 30.6 g of the acetoacetate of 3,7-dimethyl-1-octen-3-ol with b.p. 98-100° (1 mm), $n_D^{20}$ 1.4462.

The obtained acetoacetate was pyrolyzed at 180-198°. Here 1880 ml of carbon dioxide was evolved in 1.5 hours. Fractional distillation in vacuo gave 12.1 g (41%) of 6,10-dimethyl-5-undecen-2-ol with b.p. 84-85° (1 mm), $n_D^{20}$ 1.4478.

Preparation of 6,10-dimethyl-2-undecanone (hexahydropseudoionone)(XVIII). The hydrogenation of 227 g of tetrahydropseudoionone was run in a steel autoclave at room temperature over a mixed catalyst composed of 1.2 g of $PtO_2$ and 1 g of $Pd/CaCO_3$. Here 29 liters of hydrogen was absorbed in 7 hours at a hydrogen pressure of 100-20 atm. Calculated amount is 27.9 liters. Fractional distillation in vacuo gave 208 g (90%) of hexahydropseudoionone with b.p. 95-97° (4 mm), $n_D^{20}$ 1.4334.

The semicarbazone had m.p. 95-96° (from aqueous methanol) [22].

Preparation of 3,7,11-trimethyl-1-dodecyn-3-ol (XIX). A mixture of 4 liters of absolute ether and 350 g of powdered potassium hydroxide was charged into a steel reactor and after purging with nitrogen the mixture was saturated with acetylene to a pressure of 10 atm. Then 246 g of hexahydropseudoionone was added in 1.2 hours at −10°, after which the mixture was stirred for 1 hour at −10°, and for 2 hours without cooling. After the usual treatment we obtained 247 g (89%) of 3,7,11-trimethyl-1-dodecyn-3-ol with b.p. 96-98° (1 mm), $n_D^{20}$ 1.4492.

Found %: C 80.17, 80.02; H 12.67, 12.47. $C_{15}H_{28}O$. Calculated % C 80.24; H 12.62.

The 3,5-dinitrobenzoate had m.p. 47.5-48.5°

Found %: C 63.17, 63.13; H 7.20, 7.20; N 6.99, 7.10. $C_{22}H_{30}O_6N_2$. Calculated %: C 63.13; H 7.22; N 6.69.

Preparation of 3,7,11-trimethyl-1-dodecen-3-ol (XX). The hydrogenation of 119.6 g of 3,7,11-trimethyl-1-dodecyn-3-ol was run at atmospheric pressure in the presence of 0.2 g of Pd/$CaCO_3$. The hydrogenation was stopped when 12.5 liters of hydrogen had been absorbed and the acetylenic test was negative. The calculated amount of hydrogen is 13 liters. The catalyst was filtered and the filtrate was fractionally distilled in vacuo. We obtained 113.1 g (94%) of 3,7,11-trimethyl-1-dodecen-3-ol with b.p. 123-125° (6 mm), $n_D^{20}$ 1.4490.

Found %: C 78.96, 79.01; H 13.31, 13.41. $C_{15}H_{30}O$. Calculated %: C 79.64; H 13.36.

The 3,5-dinitrobenzoate is a liquid.

Hydrogenation of 3,7,11-trimethyl-1-dodecen-3-ol. The hydrogenation of 12.4 g of 3,7,11-trimethyl-1-dodecen-3-ol was run over platinum oxide at atmospheric pressure. Here 1.30 liters of hydrogen was absorbed. The calculated amount of hydrogen is 1.33 liters. After fractional distillation in vacuo we obtained 10 g of 3,7,11-trimethyl-3-dodecanol.

B.p. 127-130° (7 mm), $n_D^{20}$ 1.446, $d_4^{20}$ 0.8387, MR 72.44; calculated 72.99.

Found %: C 78.46, 78.47; H 14.11, 14.00. $C_{15}H_{32}O$. Calculated %: C 78.89; H 14.09.

The 3,5-dinitrobenzoate is a liquid.

Preparation of 6,10,14-trimethyl-5-pentadecen-2-one (XXI). Method A. a) A stream of 10.1 g (20% excess) of dry hydrogen bromide was passed without cooling into a solution of 22.6 g of 3,7,11-trimethyl-1-dodecen-3-ol in 22 ml of isooctane. After holding at room temperature for 3 hours the aqueous layer was separated, and the bromide washed with saturated bicarbonate solution, then with water, and dried over magnesium sulfate.

The crude bromide was added to a −10° solution of sodioacetoacetic ester, prepared from 2.3 g of sodium metal and 14 ml of acetoacetic ester in 60 ml of methanol. The mixture was stirred for 2 hours at −10°, for 2 hours at 0°, and then allowed to stand overnight at room temperature. The next day the mixture was stirred for 2 hours at 60° and then treated with a solution of 7 g of sodium hydroxide in 60 ml of methanol. After this the mixture was stirred at 60-70° for 4 hours, 2/3 of the methanol was distilled off, the residue diluted with water, then acidified with hydrochloric acid, and after the usual treatment we obtained 12.5 g (49%) of 6,10,14-trimethyl-5-pentadecen-2-one with b.p. 121-125° (1 mm), $n_D^{20}$ 1.4560.

Method B. A mixture of 45.6 g of 3,7,11-trimethyl-1-dodecen-3-ol and 100 ml of acetoacetic ester was heated at 170-188°. The copious evolution of carbon dioxide continued for 1.5 hours. When gas evolution had ceased the excess acetoacetic ester was distilled off, and the residue was washed with bicarbonate solution, then with water, and dried over magnesium sulfate. Two fractional distillations in vacuo gave 35.7 g (65%) of 6,10,14-trimethyl-5-pentadecen-2-one.

B.p. 132-137° (1.5 mm), $n_D^{20}$ 1.4545.

Found %: C 80.92, 80.85; H 12.62, 12.74. $C_{18}H_{34}O$. Calculated %: C 81.12; H 12.86.

Both the semicarbazone and 2,4-dinitrophenylhydrazone melted below room temperature.

Method C. Ten grams of diketene was added in 10 minutes with stirring to a mixture of 14.3 g of 3,7,11-trimethyl-1-dodecen-3-ol and 10 drops of anhydrous pyridine. The temperature of the reaction mass rose from 15 to 35°. The product was allowed to stand overnight, and the next day was subjected to pyrolysis at 130-190°. Here 1.10 liters of carbon dioxide was evolved in 30 minutes (theory is 1.42 liters). The residue was washed with 10% bicarbonate solution, then with water, and dried over magnesium sulfate. Fractional distillation in vacuo gave 7.8 g of 6,10,14-trimethyl-5-pentadecen-2-one with b.p. 127-135° (1 mm), $n_D^{20}$ 1.4545. After chromatographing on aluminum oxide we obtained 3.2 g of pure ketone (XXI) [23] with b.p. 129-130° (1 mm), $n_D^{20}$ 1.4541.

Preparation of 6,10,14-trimethyl-2-pentadecanone (XXII). The hydrogenation of 30 g of 6,10,14-trimethyl-5-pentadecen-2-one was run at atmospheric pressure in the presence of 0.75 g of platinum oxide. Here 2.62 liters of hydrogen were absorbed in 5 hours. The calculated amount of hydrogen is 2.68 liters. After filtration and fractional distillation in vacuo we obtained 28.5 g (95%) of 6,10,14-trimethyl-2-pentadecanone with b.p. 120-123° (1 mm), $n_D^{20}$ 1.4445.

The semicarbazone had m.p. 69-70° [10, 24].

Preparation of 3,7,11,15-tetramethyl-1-hexadecyn-3-ol (isophytol) (XXIII). 6,10,14-Trimethyl-2-pentadecanone (48.8 g) was added in thirty minutes to a −15° mixture of 600 ml of absolute ether, 60 g of powdered potassium hydroxide and 10 ml of anhydrous methanol, saturated with acetylene to a pressure of 12 atm. The mixture was stirred for 1 hour at −15° and then for 2 hours without cooling. After the usual treatment we obtained 47.7 g (90%) of 3,7,11,15-tetramethyl-1-hexadecyn-3-ol.

B.p. 122-125° (0.06 mm), $n_D^{20}$ 1.4543, $d_4^{20}$ 0.8525, MR 93.58; calculated 94.02.

Found %: C 81.75, 81.86; H 12.92, 13.16. $C_{20}H_{38}O$. Calculated %: C 81.50; H 13.01.

The 3,5-dinitrobenzoate is a pale yellow liquid.

Preparation of 3,7,11,15-tetramethyl-1-hexadecen-3-ol (XXIV). The hydrogenation of 39.0 g of 3,7,11,15-tetramethyl-1-hexadecyn-3-ol was run at atmospheric pressure in the presence of 0.06 g of Pd/$CaCO_3$. Here 3082 ml of hydrogen was absorbed in 2 hours, after which the acetylenic test showed negative. The calculated amount of hydrogen is 3240 ml. The catalyzate was filtered and the filtrate was fractionally distilled in vacuo. We obtained 36.8 g (84%) of 3,7,11,15-tetramethyl-1-hexadecen-3-ol.

B.p. 125-128° (0.06 mm), $n_D^{20}$ 1.4546, $d_4^{20}$ 0.8459, MR 95.04; calculated 95.61.

Found %: C 80.80, 80.82; H 13.43, 13.68. $C_{20}H_{40}O$. Calculated %: H 81.02; H 13.42

## SUMMARY

We worked out in detail the total synthesis of the isoprenoid alcohols linalool, geraniol, nerol, nerolidol, farnesol, geranyllinalool, geranylgeraniol and phytol, and also of the intermediate products of this synthesis, namely ketones and acetylenic alcohols, employing the successive repetition of the reactions of condensation of ketones with acetylene, selective hydrogenation of acetylenic alcohols, and conversion of tertiary vinyl alcohols to the isomeric primary alcohols of allylic type and unsaturated ketones of the allylacetone type.

## LITERATURE CITED

[1] I. N. Nazarov and co-workers, J. Gen. Chem. 23, 1900 (1953); Bull. Acad. Sci. USSR, Div. Chem. Sci. 1956, 960; 1956, 1370.*

[2] I. N. Nazarov and co-workers, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1946, 305.

[3] I. N. Nazarov and co-workers, J. Gen. Chem. 18, 414 (1948).

[4] M. F. Carroll, J. Chem. Soc. 1940, 704.

[5] W. Kimel and A. C. Cope, J. Am. Chem. Soc., 65, 1992 (1943).

[6] I. N. Nazarov and co-workers, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1946, 419.

[7] L. Ruzicka and G. Firmenich, Helv. Chim. Acta, 22, 392 (1939).

[8] O. Isler and co-workers, Helv. Chim. Acta, 39, 897 (1956).

[9] A. Mondon, Ber., 88, 724 (1955).

[10] F. Fischer and K. Lowenberg, Lieb. Ann., 475, 183 (1929); 464, 69 (1928).

[11] P. Karrer and co-workers, Helv. Chim. Acta, 26, 1741 (1943).

[12] J. F. Arens, and D. A. van Dorp, Rec. trav. Chim., 67, 973 (1948).

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*See C.B. Translation.

[13] L. Ruzicka and V. Fornasir, Helv. Chim. Acta 2, 182 (1919); H. Rupe and G. Lang, Helv. Chim. Acta 12, 1135 (1929).

[14] M. Busch and H. Stove, Ber. 49, 1063 (1916).

[15] H. von Soden and W. Treff, Ber. 37, 1094 (1904); 39, 906 (1906).

[16] H. Erdmann and P. Huth, J. pr. Ch. 53, 45 (1896); 56, 28 (1897).

[17] L. Ruzicka, Helv. Chem. Acta 6, 492 (1923).

[18] M. Kerschbaum, Ber. 46, 1732 (1913).

[19] I. N. Nazarov and co-workers, Proc. Acad. Sci. USSR (1957).

[20] O. Wallach, Lieb. Ann. 408, 185 (1915).

[21] P. Karrer and K. S. Yap, Helv. Chim. Acta 23, 581 (1940).

[22] N. Ishizaka, Ber. 47, 2453 (1914).

[23] U. S. Patent 2,660,608; C. A. 48, 13714c.

[24] L. I. Smith and coworkers, J. Am. Chem. Soc. 65, 1277 (1943).

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* See C.B. Translation.

# SIMPLER ANALOGS FOR CORTICOSTEROIDS

## I. STEREOCHEMISTRY OF CYANOHYDRIN AND ACETYLENIC SYNTHESIS. CONFIGURATION OF 1-CYANO- AND 1-ETHYNYL-2-METHYLCYCLOHEXANOLS

I. N. Nazarov,* A. V. Kamernitskii and A. A. Akhrem

The condensation of 2-methylcyclohexanone (I) with hydrogen cyanide and with acetylene yields in each case two stereoisomeric (crystalline and liquid) cyanohydrins (II, III) [1, 2] and acetylenic alcohols (IV, V) [3], the configuration of which, however, has not been established until now.

It seemed of interest to us to establish the spatial structure of these compounds and to trace the stereochemical course of the cyanohydrin and acetylenic syntheses in a number of substituted cyclohexanones. Of even greater interest here is the fact that studies, devoted to the stereochemistry of nucleophilic additions, do not exist in the indicated series.

To obtain crystalline derivatives of cyanohydrins (II) and (III) it seemed most convenient to saponify the nitriles to hydroxy acids, since crystalline derivatives of the cyanohydrins based on the hydroxy group cannot be obtained. However, the saponification of cyanohydrins (II) and (III) proceeds with difficulty and cannot be accomplished under ordinary conditions [2, 4, 5]. Drastic reaction conditions cause decomposition of the cyanohydrins and the regeneration of 2-methylcyclohexanone (I) [5].

Welvart [6] described the saponification of a mixture of cyanohydrins (II) and (III) in acetic acid saturated with hydrogen chloride at 20° for 7 days, followed by removal of the acetic acid by steam-distillation. Here a saponification product with m.p. 105° was obtained in 70% yield, which the author assumed was a mixture of the isomeric hydroxy acids.

We improved on the Welvart method, replacing the steam-distillation by a boiling of the reaction mass, followed by its evaporation in vacuo, and heating the residue with aqueous soda solution to decompose the unsaponified cyanohydrin. With such a procedure we obtained a nearly quantitative yield of 2-methylcyclohexanol-1-carboxylic acid (VI) with m.p. 110-111° from the crystalline cyanohydrin (II) with m.p. 53-54°, while from the liquid isomer (III) we obtained 2-methylcyclohexanol-1-carboxylic acid (VII) with m.p. 94-95°. The liquid cyanohydrin (III) is saponified with greater difficulty and requires a longer reaction time than does the crystalline isomer (II).

When the crystalline 1-ethynyl-2-methylcyclohexanol (IV) with m.p. 56-57° was oxidized with potassium permanganate we again obtained the high-melting hydroxy acid (VI) with m.p. 110-11° [3], while from the liquid 1-ethynyl-2-methylcyclohexanol (V) we obtained the low-melting hydroxy acid (VII) with m.p. 94-95°. Consequently, the formation in the cyanohydrin synthesis of two isomeric 2-methylcyclohexanone cyanohydrins (II) and (III) and their configurative relationship to acetylenic alcohols (IV) and (V) was shown.

Of the two hydroxy acids obtained (VI) and (VII), only the hydroxy acid (VI) with m.p. 110° was known before. Zernov [7] first obtained it by the bromination of trans-hexahydro-o-toluic acid (VIII) in the presence of red phophorus, followed by saponification of the obtained α-bromohexahydro-o-toluic acid (IX) with m.p. 97° using aqueous caustic. This same hydroxy acid was also obtained later by other investigators [3, 8, 9], who however failed to give any indication as to its configuration.

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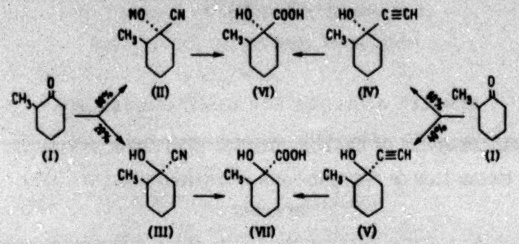
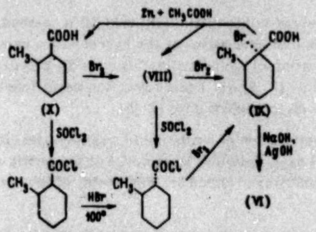


We decided to attempt the preparation of both of the isomeric α-bromohexahydro-o-toluic acids, so that by cross-saponification and on the basis of studying the stereochemistry of the bromination and reduction we could establish the spatial structure of the compounds (II-IV) and (III-V) in which we were interested. However, it proved that when the cis- and trans-hexahydro-o-toluic acids (VIII) and (X) were brominated by the Volhard-Zelinskii method only the α-bromo acid (IX), identical with the acid obtained by Zernov [7], was formed. By means of special experiments it was shown that this reaction goes through the preliminary isomerization of cis-acid (X) to the bromide of trans-acid (VIII). The saponification of bromo acid (IX), either with aqueous caustic or with moist silver oxide, leads to the same hydroxy acid (VI) with m.p. 110-111°, which indicates [10] that apparently the latter and bromo acid (IX) have the same spatial structure.



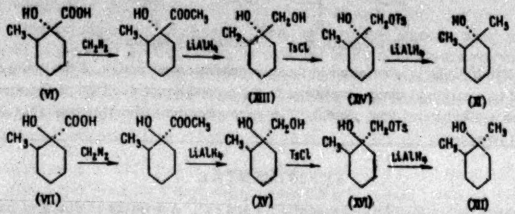
The reduction of bromo acid (IX) with zinc in acetic acid gave a mixture of the isomeric hexahydro-o-toluic acids (VIII) and (X).

As a result, the bromination of trans-acid (VII), or of its chloride, apparently proceeds with inversion of the configuration, while saponification of the α-bromo acid (IX), either with alkali or with moist silver oxide, proceeds without inversion of the configuration.

The configuration of cyanohydrins (II) and (III) and acetylenic alcohols (IV) and (V), obtained from 2-methylcyclohexanone (I), was established by their reduction to the known [11] 1,2-dimethylcyclohexanols (XI) and (XII) without affecting the asymmetric center. To accomplish this the methyl ester of hydroxy acid (VI), obtained using diazomethane, was reduced with aluminum lithium hydride in boiling ether to 1-hydroxymethyl-2-methylcyclohexanol (XIII) with m.p. 64-65°. The latter when treated with toluenesulfonyl chloride in pyridine at 0° was converted to the monotosylate (XIV), which without purification was reduced with aluminum lithium hydride by the Karrer method [12]. With such a procedure hydroxy acid (VI) gave cis-1,2-dimethylcyclohexanol (XI) with m.p. 23-24° and a known configuration [11].

A similar series of transformations was also accomplished with hydroxy acid (VII) with m.p. 94-95°. The liquid diol (XV), obtained from the methyl ester of this acid, gave the crystalline monotosylate (XVI) with m.p.

60-61°, which on reduction with aluminum lithium hydride gave the known trans-1,2-dimethylcyclohexanol (XII) with m.p. 11.5-13° [11]. In both cases the yields in all of the steps were not below 90% except in the last reaction, where the yield was 75%.

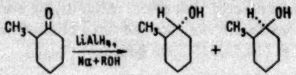


From the obtained experimental results it follows that the crystalline 1-cyano-2-methylcyclohexanol (II) and 1-ethynyl-2-methylcyclohexanol (IV), the same as their derivatives, have the side carbon chains in the cis-position, while the liquid isomers of 1-cyano-2-methylcyclohexanol (III) and 1-ethynyl-2-methylcyclohexanol (V), and also their derivatives, have the carbon chains in the trans-position.

The ratio of the isomeric cyanohydrins (II) and (III), formed in the reaction of 2-methylcyclohexanone (I) with acetone cyanohydrin, was established by saponifying a mixture of the two cyanohydrins, and it proved to be approximately equal to 4 : 1. Consequently, the cyano group adds to 2-methylcyclohexanone (I) preferentially on the side of the methyl substituent.

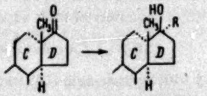
The condensation of 2-methylcyclohexanone (I) with acetylene in the presence of powdered potassium hydroxide under pressure also proceeds in a similar manner. However, in this case the reaction is less stereospecific and leads to the formation of the isomeric acetylenic alcohols (IV) and (V) in a 3 : 2 ratio.

According to the literature, the ionic reduction of 2-methylcyclohexanone (I) (using aluminum lithium hydride, sodium in alcohols, etc.), which may be regarded as a case of nucleophilic reaction at the carbonyl group [13], also proceeds with a preponderant addition of the hydrogen on the side of the methyl group; the main product obtained here is trans-2-methylcyclohexanol [14, 15].



(I) 99-64% 1-36%

It is well known that in the steroid series the addition of nucleophilic reagents (hydrogen cyanide, acetylene, alkylmagnesium halides, hydrogen, etc.) to 17-keto steroids is stereospecific with a marked preponderance of the 17 β-hydroxy compounds [16].*



R = CN, C≡CH, Alk, H.

In this case the substitutent (R) adds trans to the angular 18-methyl group, i.e. on the side of the largest substituent, which, according to Reichstein [18], is not the angular 18-methyl group but instead the 12-methylene group and the whole ring C. This finds experimental proof also in the greater ease of saponification shown by esters of 17 β-hydroxy steroids [18, 19].

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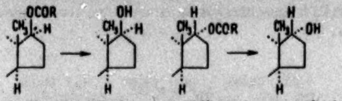
* An exception is the addition of alkylmagnesium halides to D-homo-17 α-keto steroids [17].



Easily saponified Difficultly saponified

As a result, a definite rule is manifested in the stereochemical direction of the ionic addition of acetylene and hydrocyanic acid to a carbonyl group, consisting in the preponderant addition of the entering substituent in the cis-position to the o-alkyl substituent present. The stereochemical direction probably depends on the conditions used to run such reactions.

## EXPERIMENTAL

Synthesis of 2-methyl-1-ethynylcyclohexanols (IV) and (V). A mixture of 660 g of powdered potassium hydroxide, 2.5 liters of absolute ether and 10 ml of ethanol was charged into a 6-liter steel reactor, and then with good stirring and cooling the reactor was filled in 30 minutes with acetylene to a pressure of 7 atm. Then 900 g of 2-methylcyclohexanone (b.p. 62-63° at 20 mm, $n_D^{17}$ 1.4499) was added in 6 hours with stirring. The acetylene pressure in the reactor was maintained at 7 atm during the whole experiment. The reaction was run for 10 hours. After removal of the acetylene the product was treated with 800 ml of water with efficient stirring, then neutralized with carbon dioxide, and finally dried over magnesium sulfate. After removal of the ether by distillation the residue was fractionally distilled in vacuo. We obtained 956 g of a liquid mixture of acetylenic alcohols (IV) and (V), with b.p. 76-78° (13 mm) and $n_D^{20}$ 1.4770, and 52 g of an acetylenic glycol. Long freezing of the liquid mixture led to isolation of 450 g of the cis-isomer (IV) with m.p. 56-57° (from petroleum ether) and 450 g of the liquid trans-isomer (V) with b.p. 69-70° (10 mm) and $n_D^{17}$ 1.4780. The liquid isomer (V) contains up to 10% of the crystalline alcohol. The ratio of the crystalline and liquid isomers (IV) : (V) is 60 : 40.

Oxidation of cis-1-ethynyl-2-methylcyclohexanol (IV). A solution of 15 g of potassium permanganate in 300 ml of water was added in 3 hours with vigorous stirring to a solution of 10 g of cis-1-ethynyl-2-methylcyclohexanol (IV) (m.p. 56-57°) in 100 ml of acetone, in which connection the temperature was kept below 20°. The mixture was then stirred for another hour at 20° and finally heated for an hour at 100°. The precipitate of manganese dioxide was filtered and washed with hot water. The alkaline solution was evaporated in vacuo to dryness and here 1 g of starting alcohol (IV) with m.p. 56.6-57° was isolated. The residue was washed with ether, acidified with dilute hydrochloric acid, and extracted with ether. After drying the ether extract over sodium sulfate, followed by removal of the ether by distillation, we obtained 3.5 g of cis-2-methylcyclohexanol-1-carboxylic acid (VI) as colorless crystals with m.p. 110.5-111° (from benzene) [7-9].

Found %: C 60.51, 60.46; H 8.79, 8.76. $C_8H_{14}O_3$. Calculated %: C 60.76; H 8.86.

Oxidation of trans-1-ethynyl-2-methylcyclohexanol (V). Seventeen grams of trans-1-ethynyl-2-methylcyclohexanol (V) with b.p. 76° (15 mm) was oxidized with 20 g of potassium permanganate at 22-25° in the same manner as in the preceding experiment. On evaporation we obtained 3 g of the starting alcohol and 4.8 g of acid products as a crystallizing oil. Repeated recrystallization of the latter from petroleum ether gave oxalic acid with m.p. 102°, which did not depress the melting point with an authentic specimen, and 0.5 g of trans-2-methylcyclohexanol-1-carboxylic acid (VII) as colorless needles with m.p. 94.5-95°.

Found %: C 60.66, 60.61; H 8.90, 8.84. $C_8H_{14}O_3$. Calculated %: C 60.77; H 8.86.

The mixed melting point of this acid with hydroxy acid (VI) was 72-84°.

Separation of 2-methylcyclohexanone cyanohydrins (II) and (III). The seeding and freezing of 120.5 g of mixed 2-methylcyclohexanone cyanohydrins (II) and (III) with b.p. 95.5-98° (3.5 mm), obtained by reacting 2-methylcyclohexanone with acetone cyanohydrin [1], led to the isolation of 70.5 g of crystalline cis-1-cyano-2-methylcyclohexanol (II) with m.p. 53-54° (from n-heptane) and 49 g of a liquid mixture, rich in trans-1-cyano-2-methylcyclohexanol (III).

Saponification of cis-1-cyano-2-methylcyclohexanol (II). A solution of 14 g of cis-1-cyano-2-methylcyclohexanol (m.p. 53-54°) in 60 ml of glacial acetic acid and 80 ml of concentrated hydrochloric acid was saturated with hydrogen chloride for 1 hour and then allowed to stand for 7 days at 20°. Then the solution was boiled for 5 hours under reflux, and then evaporated in vacuo. The crystalline residue was dissolved in 150 ml of saturated soda solution and then heated for 3 hours on the boiling water bath. The alkaline solution after cooling was extracted twice with ether and then acidified with dilute hydrochloric acid until strongly acid. Here an oil tending to crystallize was obtained, which was extracted with ether. The water layer was again extracted with ether in a Soxhlet apparatus for 10 hours. From the combined ether extracts, after drying over sodium sulfate and removal of the ether by distillation, we obtained 15.8 g of cis-2-methylcyclohexanol-1-carboxylic acid (VI), which after treatment with petroleum ether and recrystallization from a mixture of chloroform and n-heptane melted at 110-111°, and did not give a melting point depression when mixed with the hydroxy acid (VI) obtained from acetylenic alcohol (IV). If the reaction mass was allowed to stand only one night at 20°, with the rest of the treatment the same as before, the yield of cis-hydroxy acid (VI) was only 9.5 g.

When the hydrochloric acid and hydrogen chloride were replaced by hydrobromic acid and hydrogen bromide, and the mixture allowed to stand for 7 days, we obtained 0.5 g of a dark brown oil, from which we were unable to isolate any crystalline products.

Saponification of liquid mixture of isomeric 1-cyano-2-methylcyclohexanols (II) and (III). a) A treatment similar to the above of 14 g of liquid mixed cyanohydrins, obtained after freezing out the cis-1-cyano-2-methylcyclohexanol (II) with m.p. 53-54° and rich in the trans-isomer (III), gave 12.4 g of mixed hydroxy acids as a crystallizing oil. Recrystallization from petroleum ether gave crystals that melted at 65-80°. Fractional crystallization from petroleum ether and benzene gave 3 g of a hydroxy acid with m.p. 101-104°, which did depress the melting point when mixed with the above described cis-hydroxy acid (VI). We were unable to isolate the trans-hydroxy acid (VII) by crystallization.

b) To obtain a more accurate idea of the ratio of isomeric cyanohydrins (II) and (III), a solution of 14 g of the original mixture of cyanohydrins in 60 ml of glacial acetic acid and 80 ml of concentrated hydrochloric acid was saturated with hydrogen chloride, allowed to stand for 1.5 months at 20°, then boiled under reflux for 8.5 hours, and worked up in the usual manner. We obtained 14.7 g of mixed 2-methylcyclohexanolcarboxylic acids (VI) and (VII) with m.p. 85-93°. Fractional crystallization from a mixture of ether and petroleum ether gave 9.2 g of cis-hydroxy acid (VII) with m.p. 106-109°, which did not depress the melting point when mixed with the preceding specimen. The 5.3 g of oil isolated from the mother liquors was chromatographed on 100 ml of aluminum oxide washed with hydrochloric acid. The product was eluted successively with petroleum ether, benzene, ether, and methanol. From the ether fractions we isolated 0.4 g of trans-hydroxy acid (VII) with m.p. 92-93°, which did not give a melting point depression with the above described specimen, and 2.1 g of an oily mixture of hydroxy acids, also containing a large amount of trans-hydroxy acid (VII). From the methanol fractions we obtained an additional 2.65 g of cis-hydroxy acid (VI) with m.p. 108-110°.

Cis-$\Delta^3$-2-methylcyclohexenecarboxylic acid. A mixture of 470 g of acrylic acid (b.p. 140-141°), obtained by the Kaszuba method [20], and 750 ml of trans-piperylene was heated in the presence of hydroquinone in a 2-liter autoclave at 130° for 6 hours. After 2 vacuum-distillations we obtained 590 g of condensation product with b.p. 102-104° (2 mm). By freezing, followed by recrystallization from petroleum ether, we isolated 177.2 g of cis-$\Delta^3$-2-methylcyclohexenecarboxylic acid with m.p. 62-63° [21].

Hydrogenation of cis-$\Delta^3$-2-methylcyclohexenecarboxylic acid. A solution of 70 g of cis-$\Delta^3$-2-methylcyclohexenecarboxylic acid in 200 ml of glacial acetic acid was hydrogenated over platinum oxide at 20° and atmospheric pressure. In 8 hours 11.7 liters of hydrogen was absorbed. The catalyst was filtered and the product was fractionally distilled in vacuo. We obtained 67 g of cis-2-methylcyclohexanecarboxylic acid (X) with b.p. 98-100° (3 mm), $n_D^{20}$ 1.4641 [22].

The anilide of the acid, recrystallized from benzene had m.p. 127-128° [21, 22].

Found %: N 6.48, 6.56. $C_{14}H_{19}ON$. Calculated %: N 6.45.

Similar results were obtained when the hydrogenation was run in 95% alcohol.

Bromination of cis-2-methylcyclohexanecarboxylic acid (X). Fourteen grams of bromine was added in drops with stirring to a mixture of 7.1 g of cis-2-methylcyclohexanecarboxylic acid and 0.4 g of red phosphorus. When exothermic reaction had ceased the mixture was heated on the water bath at 54-56° for 3 hours, then for 2 hours at 100°, and finally it was allowed to stand overnight at 20°. The next day the reaction mass was washed with water and then heated with 2 volumes of formic acid (85%) on the boiling water bath for 15 minutes. The mixture was evaporated in vacuo, diluted with ether, and washed with water. After drying the ether solution over sodium sulfate, followed by removal of the ether by distillation, we obtained 11.1 g of a crystallizing oil, from which we isolated 6.5 g of crystalline 1-bromo-2-methylcyclohexanecarboxylic acid (IX) with m.p. 95-96.5° (from petroleum ether) [7].

Found %: C 43.39, 43.38; H 5.94, 5.93; Br 36.57, 36.48. $C_8H_{13}O_2Br$. Calculated %: C 43.43; H 5.93; Br. 36.11.

Reaction of bromine with cis-2-methylcyclohexanecarboxylic acid (X). Twelve grams of bromine was added with water cooling to 17.04 g of cis-2-methylcyclohexanecarboxylic acid, after which the mixture was allowed to stand for 2 hours at 20°, and then it was heated for 2 hours at 100°. Fractional distillation in vacuo gave 11 g of trans-2-methylcyclohexanecarboxyl bromide with b.p. 70-76° (5 mm). When this bromide (2.6 g) was treated with aniline (2.5 ml) in absolute benzene (10 ml) we obtained 2.8 g of the anilide of trans-2-methylcyclohexanecarboxylic acid with m.p. 152-153.5° (from benzene) [7,21, 22, 23].

Found %: N 6.27, 6.13. $C_{14}H_{19}ON$. Calculated %: N 6.45.

Reaction of thionyl chloride with cis-2-methylcyclohexane-carboxylic acid (X). A mixture of 19.2 g of cis-2-methylcyclohexanecarboxylic acid and 10 ml of thionyl chloride was kept at 20° for 1 hour, then heated for 1 hour at 100°, and finally allowed to stand overnight. The anilide, obtained from a test sample, had m.p. 126-127° (from benzene) and did not depress the mixed melting point with the anilide of authentic cis-2-methylcyclohexanecarboxylic acid [21, 22]. After heating the reaction mass at 100° for hours in a stream of dry hydrogen bromide the anilide obtained from a test sample had m.p. 151-152° (from benzene) and did not give a melting point depression with the anilide of trans-2-methylcyclohexanecarboxylic acid. When a test sample of the acid chloride was treated with aqueous caustic solution, followed by acidification and extraction with ether, we obtained trans-2-methylcyclohexanecarboxylic acid (VIII) with m.p. 51-52° (from petroleum ether) [7, 21]. The remainder of the reaction mass (about 18 g) was treated with 21.6 g of bromine and the mixture was first heated for 1 hour at 80° and then for 2 days at 100°, after which it was treated with two volumes of formic acid at 100° for 15 minutes. The formic acid was vacuum-distilled, while the residue was dissolved in ether and washed with water. After drying over sodium sulfate and removal of the ether by distillation we obtained 23.9 g of a crystallizing oil, from which we isolated 9.5 g of 1-bromo-2-methylcyclohexanecarboxylic acid (IX) with m.p. 95-97°, which did not depress the melting point when mixed with the specimen described above.

Saponification of 1-bromo-2-methylcyclohexanecarboxylic acid (IX). a) 1-Bromo-2-methylcyclohexanecarboxylic acid (2.21 g) was titrated with 0.1 N sodium hydroxide solution in the presence of phenolphthalein. The color began to disappear more slowly after 100 ml of the caustic solution had been added. Then another 212 ml of caustic solution was added and the mixture was allowed to stand overnight, after which the excess alkali was back-titrated with 0.1 N sulfuric acid solution, and this required 10 ml of acid. The solution of salts was evaporated in vacuo at 30° to a volume of 50 ml and then acidified with 1 g of concentrated sulfuric acid. After 4 extractions with ether, followed by drying over sodium sulfate and removal of the solvent by distillation, we obtained 1.5 g of crystals with m.p. 70-80°. Recrystallization from petroleum ether gave 0.8 g of hydroxy acid with m.p. 106-109°, which did not depress the melting point when mixed with cis-2-methylcyclohexanol-1-carboxylic acid (VI). In addition, we obtained 0.55 g of crystals with m.p. 87-89°, which gave a melting point depression when mixed with the cis-hydroxy acid (VI) or with the trans-hydroxy acid (VII), and were the 2-methylcyclohexenecarboxylic acid [7,8,24].

b) A solution of 2.21 g of 1-bromo-2-methylcyclohexanecarboxylic acid (IX) in 30 ml of acetone was added with stirring and water cooling to the moist silver oxide obtained from 4 g of silver nitrate. The mixture was stirred for 3 hours at 20° and then allowed to stand overnight. The next day the acetone was evaporated in vacuo, while the residue was diluted with 100 ml of water and then acidified with 100 ml of dilute hydrochloric acid. The product was extracted with ether in a Soxhlet apparatus for 20 hours and the ether extract dried over sodium sulfate. After removal of the ether by distillation we obtained 1.3 g of a crystallizing oil, from which by recrystallization from petroleum ether we isolated 0.7 g of cis-2-methylcyclohexanol-1-carboxylic acid (VI) with m.p. 109-110°. We isolated 0.5 g of an oil from the mother liquor, which could hot be made to crystallize.

Methyl ester of 1-bromo-2-methylcyclohexanecarboxylic acid. a) A dry ether solution of diazomethane (from 6 g of nitroso-methyl-urea) was added with cooling to an ether solution of 4.42 g of 1-bromo-2-methylcyclohexanecarboxylic acid (IX) and the mixture was allowed to stand for 2 hours at 20°. After removal of the ether by distillation, followed by fractional distillation on the product in vacuo, we obtained 3.7 g of the methyl ester of the bromo acid with b.p. 79-80° (3 mm), $n_D^{19}$ 1.4942.

b) A mixture of 8.2 g of the bromide of trans-2-methylcyclohexanecarboxylic acid (VIII) and 7 g of bromine was heated on the water bath for 2 hours at 70° and for 3 hours at 100°, after which the mixture was poured with cooling into 4 volumes of anhydrous methyl alcohol, alowed to stand for 2 days, diluted with 100 ml of water, and extracted 4 times with ether. The ether extract was washed with water, then with sodium sulfite solution, dried over calcium chloride, the ether distilled off, and the product fractionally distilled in vacuo. We obtained 8.5 g of the methyl ester of the bromo acid with b.p. 76-78° (2.5 mm), $n_D^{18}$ 1.4942.

Saponification of the methyl ester of 1-bromo-2-methylcyclohexanecarboxylic acid. A mixture of 11.75 g of the above described methyl ester of the bromo acid, 8 g of sodium hydroxide, 75 ml of water and 100 ml of methyl alcohol was stirred at 20° for 25 hours. Then the mixture was saturated with sodium chloride and extracted thoroughly with ether. We isolated 1 g of starting bromo acid methyl ester from the ether extract. Acidification of the alkaline solution, followed by extraction with ether, gave 5.1 g of a crystallizing oil, from which by recrystallization from petroleum ether we isolated 1.3 g of cis-2-methylcyclohexanol-1-carboxylic acid (VI) with m.p. 110-111°. The mother liquor was washed repeatedly with water (100 ml), dried over magnesium sulfate, and evaporated. We obtained 2.2 g of 2-methylcyclohexenecarboxylic acid as colorless crystals with m.p. 83-86° (from water). The water solution by extraction with ether in a Soxhlet apparatus gave 1.6 g of a crystallizing oil, from which by recrystallization from petroleum ether we obtained another 0.5 g of the cis-hydroxy acid (VI) with m.p. 901-110°. The methyl ester of the bromo acid could not be saponified with 2% aqueous sodium hydroxide solution at 20° for 18 hours.

Reduction of 1-bromo-2-methylcyclohexanecarboxylic acid (IX). A solution of 15.5 g of 1-bromo-2--methylcyclohexanecarboxylic acid in 100 ml of alcohol was treated under cooling with 13.2 g of activated zinc dust and the mixture allowed to stand overnight, after which it was refluxed for 6 hours. The zinc was filtered, washed with alcohol, the alcohol solution evaporated and residual oil washed with water, then with hydrochloric acid, and finally extracted with ether. Here an oil with a high bromine content was obtained, which was dissolved in 40 ml of glacial acetic acid, and then 13.2 g of activated zinc dust was added in portions at 5-8°. The mixture was allowed to stand overnight, after which it was heated for 1 hour on the boiling water bath. The product after cooling was extracted with ether and fractionally distilled in vacuo. Here we obtained 7.2 g of mixed stereoisomeric 2-methylcyclohexanecarboxylic acids with b.p. 105-106° (5 mm), $n_D^{20}$ 1.4635, which when treated with thionyl chloride and then aniline gave 7.8 g of a mixture of anilides with m.p. 109-113°.

Found %: N 6.65, 6.85. $C_{14}H_{19}ON$. Calculated %: N 6.45.

Repeated fractional crystallization from benzene and aqueous methyl alcohol enabled us to isolate the anilide of cis-2-methylcyclohexanecarboxylic acid (X) with m.p. 124-126° and the anilide of trans-2-methylcyclohexanecarboxylic acid (VIII) with m.p. 149-151°, neither of which gave a melting point depression when mixed with the authentic specimens.

Methyl ester of cis-2-methylcyclohexanol-1-carboxylic acid. An ether solution of diazomethane (from 12 g of nitroso-methyl-urea) was added to a solution of 15.8 g of cis-2-methylcyclohexanol-1-carboxylic acid (VI) in 100 ml of ether and the mixture allowed to stand for 2 hours at 20°. The product was washed with saturated sodium bicarbonate solution, dried over sodium sulfate, and vacuum-distilled. We obtained 10.8 g of the methyl ester of cis-2-methylcyclohexanol-1-carboxylic acid with b.p. 66° (3 mm), $n_D^{20}$ 1.4620.

Found %: C 62.48, 62.58; H 9.37, 9.46. $C_9H_{16}O_3$. Calculated %: C 62.74; H. 9.37.

Reduction of the methyl ester of cis-2-methylcyclohexanol-1-carboxylic acid. A solution of 10.4 g of the methyl ester of cis-2-methylcyclohexanol-1-carboxylic acid in 50 ml of absolute ether was added with stirring to a solution of 4.5 g of aluminum lithium hydride in 300 ml of absolute ether. When exothermic reaction had ceased the mixture was refluxed on the water bath for 11 hours, then 15 ml of ethyl acetate was added, the mixture was acidified with dilute sulfuric acid until acid to litmus and then neutralized with solid sodium bicarbonate. The ether solution after drying and fractional distillation gave 8.3 g of cis-1-hydroxymethyl-2-methylcyclohexanol (XIII) with m.p. 64-65° (from petroleum ether).

Found %: C 66.58, 66.52; H 11.22, 11.08. $C_8H_{16}O_2$. Calculated %: C 66.67; H 11.11.

Preparation and reduction of monotosylate of cis-1-hydroxymethyl-2-methylcyclohexanol (XIV). A solution of 6.3 g of cis-1-hydroxymethyl-2-methylcyclohexanol (XIII) in 45 ml of absolute pyridine was cooled to 0° and then 10 g of toluenesulfonyl chloride was added in portions with stirring. The mixture was allowed to stand overnight at 0°, after which 100 ml of saturated sodium bicarbonate solution was added, the product extracted with ether, the ether extract washed with dilute sulfuric acid, then with saturated sodium bicarbonate solution, and dried over sodium sulfate. After distilling off the solvent in vacuo we obtained 14.5 g of the tosylate (XIV) as a brown oil, which could not be made to crystallize.

A solution of 16 g of the above described crude tosylate (XIV) in 70 ml of absolute ether and 70 ml of absolute benzene was added with stirring to a suspension of 6 g of aluminum lithium hydride in 150 ml of absolute ether and 150 ml of absolute benzene. The mixture was boiled under reflux for 20 hours, after which 30 ml of ethyl acetate was added, and the mixture first acidified with dilute sulfuric acid and then neutralized with solid sodium bicarbonate. After the usual treatment and fractional distillation in vacuo we obtained 5 g of cis-1,2-dimethylcyclohexanol (XI) with b.p. 73-75° (18 mm), $n^{20}_D$ 1.4649, and m.p. 23.5-24° (from petroleum ether).

Found %: C 74.43, 74.54; H 12.46, 12.63. $C_8H_{16}O$. Calculated %: C 74.92; H 12.50.

Literature [11]: h p. 23.2°, b.p. 82-85° (25 mm), $n^{20}_{5015}$ 1.4649.

Methyl ester of trans-2-methylcyclohexanol-1-carboxylic acid. An ether solution of diazomethane (from 14 g of nitroso-methyl-urea) was added with cooling to an ether solution of 10.9 g of trans-2-methylcyclohexanol-1-carboxylic acid (VII) (m.p. 94-95°) and the mixture allowed to stand for 3 hours at 20°. After the usual treatment and fractional distillation in vacuo we obtained 11.3 g of the methyl ester of trans-2-methylcyclohexanol-1-carboxylic acid with b.p. 56° (3 mm), $n^{20}_D$ 1.4535.

Found %: C 62.75, 62.84; H 9.45, 9.35. $C_9H_{16}O_3$. Calculated %: C 62.74; H 9.37.

Reduction of the methyl ester of trans-2-methylcyclohexanol-1-carboxylic acid. The reduction of 10.6 g of the methyl ester of trans-2-methylcyclohexanol-1-carboxylic acid with 4.5 g of aluminum lithium hydride was run in the same manner as described before, but the boiling time was increased to 23 hours. Fractional distillation in vacuo gave 8.3 g of trans-1-hydroxymethyl-2-methylcyclohexanol (XV) with b.p. 97° (3 mm), $n^{20}_D$ 1.4890.

Found %: C 66.67, 66.48, H 10.90, 11.00. $C_8H_{16}O_2$. Calculated %: C 66.67; H 11.11.

Preparation and reduction of the monotosylate of trans-1-hydroxymethyl-2-methylcyclohexanol (XVI). Toluenesulfonyl chloride (13.5 g) was added in portions at 0° to a solution of 8.2 g of trans-1-hydroxymethyl-2-methylcyclohexanol (XV) in 40 ml of anhydrous pyridine. The mixture was allowed to stand at 0° for 2 days and then was worked up in the manner described above. We obtained 17.2 g of the tosylate (XVI) as a crystallizing oil. Recrystallization of a portion of the latter from a mixture of benzene and petroleum ether gave crystals with m.p. 60-61°.

Found %: C 60.51, 60.44; H 7.36, 7.36; S 10.70, 10.89. $C_{15}H_{22}O_4S$. Calculated %: C 60.37; H 7.44; S 10.73.

A solution of 16.6 g of crude tosylate (XVI) in 100 ml of absolute benzene was added to a suspension of 6.8 g of aluminum lithium hydride in 220 ml of absolute ether and 120 ml of absolute benzene, after which the mixture was refluxed for 23 hours and then decomposed with 45 ml of ethyl acetate. Here we obtained 4.4 g of trans-1,2-dimethylcyclohexanol (XII) with b.p. 71.5° (25 mm), $n^{20}_D$ 1.4610, and m.p. 11-13°.

Found %: C 74.60, 74.40; H 12.48, 12.45. $C_8H_{16}O$. Calculated %: C 74.92; H 12.50.

Literature [11]: b.p. 13.2°, b.p. 74° (25 mm), $n^{20}_{5015}$ 1.4614.

## SUMMARY

The stereochemistry of the addition of hydrogen cyanide and of acetylene to 2-methylcyclohexanone was studied, and the configuration of the resulting 1-cyano-2-methylcyclohexanols, 1-ethynyl-2-methylcyclohexanols and their derivatives (hydroxy acids, ketols, keto diols, etc.) was established.

## LITERATURE CITED

[1] I. N. Nazarov, A. A. Akhrem and A. V. Kamernitskii, J. Gen. Chem. 25, 1345 (1955).*

[2] B. Tchoubar, Bull.Chim. Soc. 1949, 160.

[3] J. D. Billimoria, J. Chem. Soc. 1953, 2626.

[4] K. Auwers and F. Krollpfeiffer, Ber. 48, 1389 (1915).

[5] M. Godchot and G. Cauquil, C. r. 206, 1523 (1938).

[6] Z. Welvart, Bull. Soc. Chim. 1949, 331.

[7] W. Zernov, Ber., 32 1169 (1899).

[8] F. W. Kay and W. H. Perkin, J. Chem. Soc., 87, 1066 (1905).

[9] M. Passerini, Gazz., 53, 415 (1923).

[10] C. R. Ingold, Structure and mechanism in organic Chemistry, N. Y., 387 (1953).

[11] G. Chiurdoglu, Bull. Soc. Chim. Belg., 47, 241 (1938); G. Chiurdoglu and A. Guillemonat, Bull Soc. Chim., (5) 5, 1328 (1938).

[12] H. Schmid and P. Karrer, Helv. Chim. Acta, 32, 1371 (1949).

[13] See [10], p. 700.

[14] P. Anziani and R. Cornubert, Bull. Soc. Chim. 12, 359 (1945).

[15] D. S. Novce and D. B. Denney, J. Am. Chem. Soc., 72, 5743 (1950).

[16] I. N. Nazarov and L. D. Bergel'son, Chemistry of Steroid Hormones [in Russian] (Moscow, 1955); L. Fieser and M. Fieser, The Chemistry of Natural Products Related to Phenanthrene [Russian translation] (Moscow, 1953).

[17] L. Ruzicka, Nagi Wahba, P. T. Herzig, and H. Heusser, Ber., 85, 491 (1952); R. B. Turner, R. Anliker, R. Helbling, J. Meier, and H. Heusser, Helv. Chim. Acta, 38, 411 (1955).

[18] J. von Euw and T. Reichstein, Helv. Chim. Acta, 30, 205 (1947).

[19] H. Heusser, K Meier, and L. Ruzicka, Helv. Chim. Acta, 29, 1250 (1946).

[20] F. J. Kaszuba, J Am. Chem. Soc., 67, 1227 (1945).

[21] K. Alder and W. Vogt, Lieb. Ann., 564, 120, (1949).

[22] A. K. Macbeth, J. A. Mills, and D. H. Simmonds, J. Chem. Soc., 1949, 1011.

[23] A. Skita, H. Hauber, and R. Schonfelder, Lieb, Ann., 431, 1 (1923).

[24] F. P. Mazza and A. Cremona, Gazz., 56, 318 (1927).

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*See C.B. Translation.

# INVESTIGATIONS IN THE FIELD OF POLYMETHYLENE RINGS

## XXX. REACTION OF DIACETYL AND DIBENZOYL WITH DIMETHYLHYDRAZINE

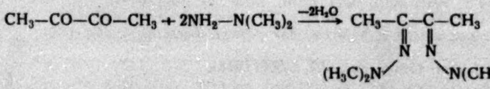
N. A. Domnin, V. I. Diurnbaum, and V. A. Cherkasova

It was shown by us that cyclopentanedione-1,2, cyclohexanediones-1,2 and -1,4 [1], and also pentanedione-2,4 (acetylacetone) [2], and hexanedione-2,5 (acetonylacetone) [3], readily give stable mono- and bis-dimethylhydrazones on reaction with dimethylhydrazine. In contrast to the enumerated diketones, cyclohexanedione-1,3 and 5,5-dimethylcyclohexanedione-1,3 (dimedon), and also dibenzoylmethane, reacting under the same conditions with dimethylhydrazine, give only monodimethylhydrazones and do not give bisdimethylhydrazones at all.

At the same time it was established by us that of all the dihydrazones obtained, the most unstable are those of cyclopentanedione-1,2 and cyclohexanedione-1,2. These facts were explained by us on the basis of the structure of the five- and six-membered rings and the steric hindrances resulting from the presence of $=N-NH_2$ and $=N-N(CH_3)_2$ groups in these cyclic dihydrazones.

For further generalization of the facts obtained, however, it was necessary to carry out a comparative study of the reactions of the simplest aliphatic and aliphatic-aromatic 1,2-diketones with dimethyldrazine. For this purpose we also studied the reactions of diacetyl and dibenzoyl with dimethylhydrazine. With regard to this it should be noted that the reactions of diacetyl and dibenzoyl with hydrazine were studied by other investigators [4], while those with dimethylhydrazine have not been studied at all. Furthermore and to the point, as has been repeatedly shown, the reactions of the different diketones with hydrazine and dimethylhydrazine proceed quite differently, resulting in dissimilar products [1-3, 5].

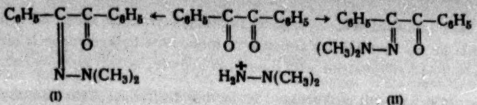
The reaction of diacetyl with dimethylhydrazine takes place even at room temperature; however, a purer bisdimethylhydrazone was obtained after heating and stirring the mixture for 6 hours in a water bath at 60-70°. The reaction goes according to the scheme



$$CH_3-CO-CO-CH_3 + 2NH_2-N(CH_3)_2 \xrightarrow{-2H_2O} CH_3-\underset{\underset{(H_3C)_2N-N}{\|}}{C}-\underset{\underset{N-N(CH_3)_2}{\|}}{C}-CH_3$$

Of the three possible geometric forms, the bisdimethylhydrazone is obtained only in one, the most probable anti-anti-form, in which two $N(CH_3)_2$ groups are directed toward opposite sides and lie at the maximum distance from one another.

The reaction of dibenzoyl (benzil) with dimethylhydrazine also takes place at room temperature; in this case crystals of the monodimethylhydrazone separate out from the solution within a day. However, the reaction goes more completely and more rapidly when the mixture is heated in a water bath at 80-90° for 2 hours. After removal of solvent, crystals of the monodimethylhydrazone are isolated, which after recrystallization from alcohol separate out in two forms, one the α- or syn-form (I), m.p. 99°, and the other the β- or anti-form (II), m.p. 86°. The reaction goes according to the scheme



$$C_6H_5-\underset{\underset{N-N(CH_3)_2}{\|}}{C}-\underset{\underset{O}{\|}}{C}-C_6H_5 \leftarrow C_6H_5-\underset{\underset{O}{\|}}{C}-\underset{\underset{O}{\|}}{C}-C_6H_5 \quad H_3\overset{+}{N}-N(CH_3)_2 \rightarrow C_6H_5-\underset{\underset{(CH_3)_2N-N}{\|}}{C}-\underset{\underset{O}{\|}}{C}-C_6H_5$$

(I) (II)

An x-ray diffraction investigation of the structures of the obtained geometric forms of the monodimethylhydrazone was conducted, which indicated the presence of polymorphism due to stereoisomerism.

The characteristics of the syn- and anti-form crystals are given in Table 2 in the experimental part.

However, only a complete study of diffraction densities can give an answer to the question of the structure of these geometric forms.

A spectrophotometric investigation of the stereoisomers ($\alpha$- and $\beta$-forms) in the 3-12 $\mu$ infrared region was conducted with an IKS-11 spectrometer which had a NaCl prism. Clear absorption maxima were obtained in the 1650-1672 $cm^{-1}$ region, corresponding to the valence vibrations of the carbonyl group in the $\beta$-form [9]. For the $\alpha$-form in oil this wave number was faint (1642-1661 $cm^{-1}$), which was probably due to screening of the carbonyl group by methyl groups or by formation of a hydrogen bond between the carbonyl oxygen and a methyl hydrogen. Analysis of the rest of the spectrum shows that for the $\alpha$- and $\beta$-forms, characteristic absorption maxima may be distinguished, which are exactly repeated for the given form, in spectra taken in oil and in $CCl_4$ solution. There are three regions for the $\alpha$-form: 1053-1063, 923, and 874-875 $cm^{-1}$. There is one region for the $\beta$-form: 965-967 $cm^{-1}$.

In order to gain an understanding of the comparative characteristics of the spectra, the wave numbers for the most pronounced absorption maxima are listed in Table 1, the table being compiled in such a way that identical or similar numbers for different spectra lie on the same line.

We attempted to carry out the reaction of the monodimethylhydrazone with a second molecule of dimethylhydrazine to form the bisdimethylhydrazone, under various conditions, but without success. It turned out that the free carbonyl group of the benzil monodimethylhydrazone molecule reacts neither with dimethylhydrazine, nor with hydroxylamine, nor with hydrazine hydrate.

TABLE 1

Wave Numbers for the Most Pronounced Absorption Maxima in the Infrared Spectra*

| $\alpha$-Form | | $\beta$-Form | | 1-Methyl-3,4-diphenylpyrazole | Characteristics of vibrations for groups [9, 10] |
|---|---|---|---|---|---|
| in oil | in $CCl_4$, solution | in oil | in $CCl_4$ solution | | |
| 2959 (v.s.) | 2890 (v.s.) | 2890 (v.s.) | 2907 (v.s.) | | $CH_3$ |
| 1642 (w) | 1661 (s.) | 1651 (s.) | 1672 (s.) | | C=O |
| 1567 (w.) | 1558 (s.) | 1558 (w.) | 1558 (s.) | | C=N |
| 1456 (v.s.) | 1445 (s.) | 1453 (s.) | 1453 (v.s.) | 1464 (s.) | $CH_3$ |
| 1387 (s.) | | 1381 (s.) | | 1385 (s.) | — |
| 1063 (s.) | 1053 (s.) | | 1080 (w.) | 1068 (s.) | $CH_3$ |
| 1016 (av.) | 1020 (av.) | 1020 (w.) | 1022 (av.) | 1020 (av.) | $CH_3$ |
| | | 965 (s.) | 967 (s.) | 955 (s.) | — |
| 923 (s.) | 923 (s.) | 915 (av.) | 917 (av.) | 917 (av.) | C—C |
| 874 (s.) | 875 (s.) | | | | — |
| | | | | 852 (w.) | N—N |
| | | | | 825 (s.) | C—H |

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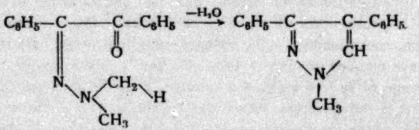
* The following abbreviations are used to denote the intensity of absorption: v.s. – very strong, s. – strong, av. – average, w. – weak.

On treatment of benzil monodimethylhydrazone with hydroxylamine under the conditions in which benzildioxime is formed [6], no reaction takes place and the monodimethylhydrazone is recovered unchanged. On treatment of benzil monodimethylhydrazone with hydrazine hydrate, benzil monohydrazone is obtained.

None of the attempts at synthesis of dibenzoyl bisdimethylhydrazone from dimethylhydrazine and benzil led to substitution of the second carbonyl group. As a result of a reaction carried out in alcoholic solution in sealed tubes which were heated for 5 hours at 100-110°, there was obtained a cyclization product of benzil monodimethylhydrazone – 1-methyl-3,4-diphenylpyrazole. The latter was also obtained simply by heating the crystalline monodimethylhydrazone in sealed tubes.

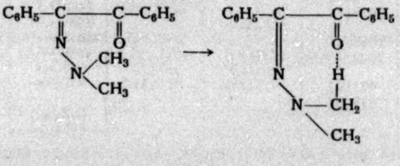
The formation of 1-methyl-3,4-diphenylpyrazole from benzil monodimethylhydrazone probably takes place according to the scheme



The experimental data obtained and the facts established give grounds for the assumption that the addition of 1 molecule of dimethylhydrazine to benzil to form the monodimethylhydrazone leads to a molecular structure in which the reaction of the second carbonyl group of the benzil with dimethylhydrazine is hindered. This may be explained more definitely by the fact that the two methyl groups bound to the nitrogen atom fill the space between the two phenyl groups quite closely, thus creating steric hindrances which make it impossible for dimethylhydrazine molecules to approach the remaining carbonyl group in the monodimethylhydrazone molecule. These steric hindrances may be interpreted as purely mechanical ones due to filling of the space, or they may be the result of the mutual influence of the atoms in the molecule, electron shifts, and effects which are for the present a matter of ideas and assumptions of a purely qualitative character. It will be possible to take up the description of these phenomena from the quantitative side only after the accumulation of more extensive factual and experimental material.

It was established earlier by us [1, 5] that cyclohexanedione-1,3 and dimedon, and also dibenzoylmethane, can form only monodimethylhydrazones, and are quite incapable of forming bisdimethylhydrazones. In all these cases we attempted to explain the inertness of the second carbonyl group in the molecules of the stated diketones by their capacity for enolization; however, we were unable to overcome the contradictions encountered in this problem.

One more possible hypothesis for explanation of the inertness of the carbonyl group in molecules of the monodimethylhydrazones of the diketones under discussion should be considered quite probable – this is the idea of the possibility of formation of a hydrogen bond between the carbonyl group and a hydrogen of a methyl group bound to a nitrogen atom, according to the scheme



In this case, of the two geometric forms of benzil monodimethylhydrazone, only the syn-form can give a hydrogen bond, while the anti-form must not be free to form a hydrogen bond.

This problem will be studied in continuing investigations of the hydrazones of cyclic diketones.

## EXPERIMENTAL

It was necessary to dry the brown, technical dimethylhydrazine for several days over potassium hydroxide and to collect the fraction boiling from 55 to 56° in the first distillation. This clear fraction was dried again over potassium hydroxide and distilled, the fraction boiling from 62 to 64° being collected. This preliminary purification of the technical dimethylhydrazine, as we found out, is very important for its reaction with diketones and the purity of the products obtained.

Synthesis of diacetyl bisdimethylhydrazone. Into a three-neck, round-bottomed flask, provided with a mechanical stirrer, a reflux condenser, and a dropping funnel, was put 18 g (0.3 mole) of freahly distilled dimethylhydrazine (about 5-10% excess) in 20 ml of anhydrous ethyl alcohol. A solution of 8.6 g (0.1 mole) of diacetyl in 10 ml of anhydrous alcohol was introduced into the flask through a dropping funnel. The mixture was heated for 6 hours in a water bath at 60-70°. As a result there was obtained a clear, yellow solution, from which the alcohol was distilled at 50° and 200 mm pressure. The residue was fractionated in vacuo.

B.p. 70-72° (5 mm), $d_4^{20}$ 0.9213, $n_D^{20}$ 1.4940, $MR_D$ 53.72; calculated 51.33.

Found %: C 56.78, 56.46; H 10.45, 10.39; N 33.28, 32.96, M 165.8, 163.3. $C_8H_{18}N_4$. Calculated %: C 56.47; H 10.58; N 33.28, M 170.

Synthesis of benzil monodimethylhydrazone. Benzoin and benzil were prepared according to Adams and Marvel [7] and Clark and Drepser [8]. After recrystallization from carbon tetrachloride, m.p. 93°; yield, 89%.

To a solution of 21 g (0.1 mole) of benzil in 63 ml of anhydrous alcohol was added 9 g (0.15 mole) of freshly distilled dimethylhydrazine. After heating in a water bath at 80-90° for 2 hours, the mixture was transferred to a Wurtz flask, and the bulk of the alcohol was distilled off in vacuo at 20-30°. The light-yellow precipitate thus formed had an indefinite melting point from 60-70° after drying. There was obtained 22 g (87 7%) of the substance. On recrystallization from alcohol there were obtained crystals of two forms, the larges and most characteristic crystals of which were mechanically withdrawn and studied separately.

α-Form. The clear, white crystals, twice recrystallized from anhydrous alcohol, had m.p. 99°. The substance was soluble in alcohol, ether, benzene, dioxane, and carbon tetrachloride and insoluble in water or alkalis either in the cold or on heating. On standing in air it was stable and did not change.

Found %: N 11.24, 11.25, M 235.3, 240.7. $C_{16}H_{16}ON_2$. Calculated %: N 11.11, M 252.

β-Form. Fine, bright-yellow crystals with m.p. 86°, having greater solubility than the α-form in the same solvents; like the α-form, they were insoluble in water and alkalis and stable on standing. The melting point, after two recrystallizations from anhydrous alcohol, was 86°.

Found %: N 11.32, 11.01. M 237.3, 244.6. $C_{16}H_{16}ON_2$. Calculated %: N 11.11, M 252.

On the basis of X-ray diffraction data the diffraction densities for the two stereoisomeric α- and β-forms of benzil monodimethylhydrazone were calculated. For comparative characteristics pycnometric densities ($d_4^{20}$) were experimentally determined: the value for the α-form was 1.199 and that for the β-form 1.156.

The X-ray diffraction data are given in Table 2.

Spectrophotometric investigation of the α- and β-forms of benzil monodimethylhydrazone in the infrared region. The first absorption spectrum was taken for the α-form (m.p. 99°) in vaseline oil: 17% of the oil, 0.02 mm layer. The data of interpretation are shown in Figure 1.

The second absorption spectrum for the α-from was taken in $CCl_4$ solution: 1% solution, 0.5 mm layer. The results of interpretation are shown in Figure 2.

The third absorption spectrum was taken for the β-form (m.p. 86°) in vaseline oil: 20% of the oil, 0.2 mm layer. Results are shown in Figure 3.

The fourth absorption spectrum was taken for the β-form in $CCl_4$ solution: 6% solution, 0.5 mm layer. Results are shown in Figure 4.

The absorption maxima in the infrared region of the spectrum for the α- and β-forms of benzil monodimethylhydrazone in oil and in $CCl_4$ solution are listed below.

TABLE 2

| Characteristic | Yellow modification, β-anti-form | Colorless modification, α-syn-form |
|---|---|---|
| Melting point | 86° | 99° |
| Laue class | $\frac{2}{m}$ | $\frac{2}{m}$ |
| Syngony | Monoclinic | Monoclinic |
| Diffraction group | $3;\ \frac{2}{m}P\frac{2_1}{-}\boxed{\kappa}$ | $3;\ \frac{2}{m}P\frac{2_1}{-}\boxed{\kappa}$ |
| Space group | $P\frac{2_1}{m}$ or $P2_1$ | $P\frac{2_1}{m}$ or $P2_1$ |
| Unit-cell dimensions *a* | 11.48 кX | 8.12 кX |
| *b* | 8.47 кX | 15.13 кX |
| *c* | 14.30 кX | 11.34 кX |
| β | 90° | 78°35′ |
| Pycnometric density | 1.156 g/cm$^3$ | 1.199 g/cm$^3$ |
| X-ray diffraction density | 1.172 g/cm$^3$ | 1.195 g/cm$^3$ |
| Unit-cell volume | 1420 кX$^3$ | 1380 кX$^3$ |
| Number of molecules [formula units] per unit cell | 4 (3.95) | 4 (3.95) |

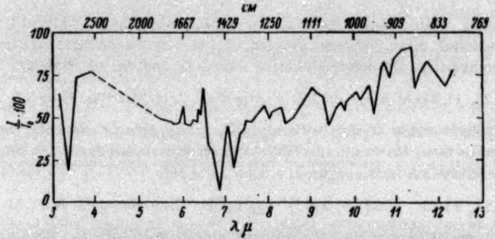


Fig. 1. Transmission curve of the α-form of benzil monodimethylhydrazone in oil.

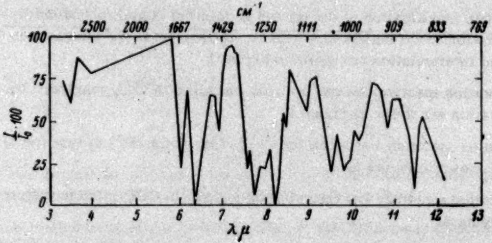


Fig. 2. Transmission curve of the α-form of benzil monodimethylhydrazone in CCl$_4$ solution.

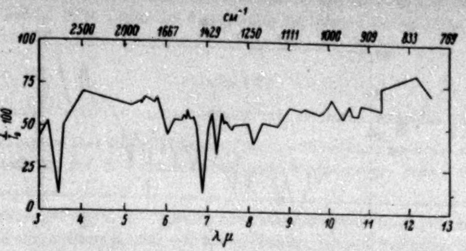


Fig. 3. Transmission curve of the β-form of benzil monodimethylhydrazone in oil.

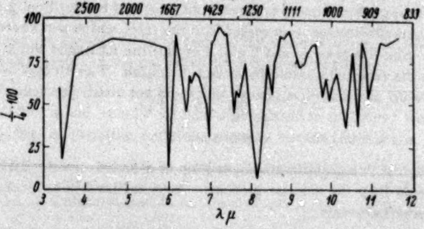


Fig. 4. Transmission curve of the β-form of benzil monodimethylhydrazone in $CCl_4$ solution.

α-Form in oil: 3.38 (v. s.), 5.92 (av.), 6.09 (w.), 6.38 (w.), 6.87 (v. s.), 7.22 (s.), 7.59 (w.), 8.04 (av.), 8.40 (w.), 9.42 (s.), 9.84 (av.), 10.24 (s.), 11.44 (s.).

α-Form in $CCl_2$ solution: 3.46 (v. s.), 6.02 (s.), 6.42 (s.),6.92 (s.), 7.55 (w.), 7.72 (w.), 8.47 (w.), 9 50 (s.), 9.80 (s.), 10.84 (s.), 11.43 (s.).

β-Form in oil: 3.46 (v. s.), 6.06 (s.), 6.42 (w.), 6.58 (av.), 6.88 (s.), 7.24 (s.), 7.60 (w.), 8.16 (av.), 9.80 (w.), 10.36 (s.), 10.71 (av.), 10.92 (av.).

β-Form in $CCl_4$ solution: 3.44 (v. s.), 5.98 (s.), 6.42 (s.), 6.54 (av.), 6.88 (v. s.), 7.55 (av.), 7.68 (w.), 8.16 (av.), 8.52 (s.), 9.26 (w.), 9.78 (av.), 9.94 (av.), 10.34 (s.), 10.64 (s.), 10.90 (av.).

Decomposition of benzil monodimethylhydrazone. To 2.5 g of benzil monodimethylhydrazone (unrecrystallized product) was added 30 ml of 10% hydrochloric acid. The substance dissolved after a while, and on standing, a white, acicular precipitate (about 2 g) formed, which, after recrystallization from anhydrous alcohol, had m.p. 96°. A test combustion revealed the absence of nitrogen in the substance. A mixture test with known benzil gave no depression.

Action of hydrazine hydrate on benzil monodimethylhydrazone. To 2.5 g (0.1 mole) of benzil monodimethylhydrazone in 12 ml of anhydrous alcohol was added 0.75 g (0.15 mole) of hydrazine hydrate in 3 ml of alcohol. The mixture was boiled in a water bath for 5 hours. From the cooled solution, 1.85 g of a white, crystalline precipitate separated out. After recrystallization from alcohol the substance had m.p. 150-151°. A mixture test with known benzil monohydrazone showed no depression.

Conversion of benzil monodimethylhydrazone to 1-methyl-3,4-diphenylpyrazole. To 7 g of benzil in 21 ml of anhydrous alcohol was added 5 g of dimethylhydrazine. The mixture was heated in a water bath for

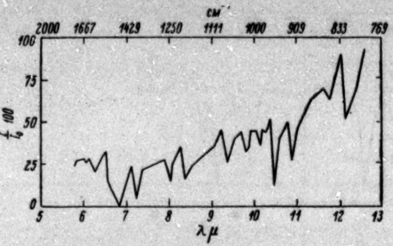


Fig. 5. Transmission curve of 1-methyl-3,4-diphenyl- pyrazole in oil.

10 hours at 85-90° and left overnight. On recrystallization of the precipitate formed, only benzil monodimethylhydrazone was found. For the purpose of seeking the conditions for the synthesis of benzil bisdimethylhydrazone, the reaction of benzil with dimethylhydrazine was carried out in sealed tubes. Five g of benzil, 10 ml of anhydrous alcohol, and 3 g of dimethylhydrazine were sealed into the tube, which was heated in an oven at 100-110° for 5 hours. After 2 days the tube was opened, and 2 g of a crystalline substance which was recrystallized and had m.p. 160°, was isolated from the reaction mixture by suction filtration. The alcohol was distilled off from the filtrate; in the residue a yellow oil of unknown structure, which did not distill in vacuo, was obtained. Carrying out the experiment under the same conditions of heating in a tube for 5 hours, but at 120-130°, leads mainly to the same product with m.p. 160° and a small amount of a new substance with m.p. 114-115°.

On heating 10 g of benzil with 6 g of dimethylhydrazine in a sealed tube for 10 hours at 150-160°, three distinct substances were isolated from the reaction products. Recrystallized from alcohol, they had m. p. 160° (about 3 g), 114°, and 232° (small amounts).

Substance with m.p. 160°. Found %: C 81.93, 81.78; H 6.19, 6.04, N 11.94, 12.09. M 219.8, 221.5. $C_{16}H_{14}N_2$. Calculated %: C 82.05; H 5.98; N 11.96, M 234.

On the basis of analyses, molecular weight, and the results of a spectrophotometric study of the infrared spectra of the substance obtained, the structure of 1-methyl-3,4-diphenylpyrazole should be assigned to it.

With NaCl prism, the 3-12 μ region was taken in vaseline oil: 33% paste, 0.04 mm layer. Results are shown in Figure 5. The following absorption maxima were found in the infrared region of the spectrum for 1-methyl-3,4-diphenylpyrazole in oil: 6.83 (s.), 7.22 (s.), 8.05 (w.), 8.38 (w.), 9.36 (s.), 9.80 (av.), 10.14 (av.), 10.47 (s.), 10.90 (av.), 11.74 (w.), 12.12 (s.).

Substance with m.p. 114°. Found %: C 83.68, 83.78; H 5.35, 5.26; N 5.00, 5.06. $C_{20}H_{15}ON$. Calculated %: C 83.79; H 4.93; N 4.93.

The structure of this substance remained unknown; it was not possible to determine even its molecular weight.

Substance with m.p. 232°. Found %: C 78.60, 78.37; H 6.46, 6.50; N 4.70, 4.57. $C_{29}H_{20}ON_2$. Calculated %: C 78.43; H 6.53; N 4.57.

The molecular weight could not be determined; the structure of the substance remained unknown.

Into one of the tubes of a Terent'ev reactor was put 2 g of the monodimethylhydrazone, and into the other was put 2 g of anhydrous cupric sulfate. After heating for one-half hour in an oil bath at 120-130°, the monodimethylhydrazone became distended, and crystals separated out from the molten mass. After recrystallization from alcohol there was obtained 1.45 g (73%) of a clear, crystalline product with m.p. 160°, which proved to be 1-methyl-3,4-diphenylpyrazole and which was readily soluble in alcohol, benzene, and ether and insoluble in cold and hot water and in alkalis. When it was added to 10% hydrochloric acid, it dissolved rapidly and spontaneously. Alkalinization of the solution caused formation of a white, flocculent precipitate which, after washing with water and alcohol, had m.p. 160°.

In conclusion we consider it a pleasant duty to express our sincere thanks to E. V. Stroganov for the X-ray structural investigation and to D. N. Glebovskii for recording the infrared spectra of the compounds obtained by us.

## SUMMARY

1. Diacetyl bisdimethylhydrazone has been obtained and characterized for the first time.

2. It has been established that dibenzoyl (benzil) reacts with only one molecule of dimethylhydrazine and thereby gives two steric α- and β-forms of the monodimethylhydrazone. Both of these forms have been characterized.

3. It has been established that benzil does not form bisdimethylhydrazones and that the carbonyl group of the monodimethylhydrazone reacts neither with hydroxylamine, nor with hydrazine, nor with dimethylhydrazine.

4. It has been established that when benzil monodimethylhydrazone reacts with hydrazine hydrate, benzil hydrazone is obtained.

5. It has been established that on heating, benzil monodimethylhydrazone cyclizes to 1-methyl-3,4-diphenylpyrazole.

6. The facts obtained are explained in the light of the steric structures of the mono- and bisdimethylhydrazone molecules and the steric hindrances which arise in these molecules.

## LITERATURE CITED

[1] N A. Domnin and N. S. Glebovskaia, J. Gen. Chem. 27, 665 (1957).*

[2] N. A. Domnin, Wang Hsu-k'un and N. S. Glebovskaia, J. Gen. Chem. 27, 1512 (1957).*

[3] N. A. Domnin, M. N. Zelenina, and N. S. Glebovskaia, J. Gen. Chem. 27, 1516 (1957).*

[4] T. Curtius and K. Thun, J. pr. Ch., (2) 44, 174 (1891).

[5] N. A. Domnin and N. S Glebovskaia, J. Gen. Chem. 27, 656 (1957).*

[6] K. Anwers and V. Meyer, Ber., 21, 3510 (1888); 22, 537 (1889).

[7] Synth. Org. Preps. 1, 95 (1949).**

[8] Synth. Org. Preps, 1, 90 (1949).**

[9] L. J. Bellamy, The Infrared Spectra of Complex Molecules, London (1954).

[10] L. Brownlie, J. Chem. Soc. 1950, 3062.

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Leningrad State University.

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*Original Russian pagination. See C.B. Translation.

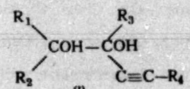
**In Russian.

# INVESTIGATION OF TRANSFORMATIONS OF PINACOLS WITH SUBSTITUTED ACETYLENIC RADICALS

## XVI. SYNTHESIS AND TRANSFORMATIONS OF SYM. DIMETHYLPHENYL(TERT-BUTYLETHYNYL)ETHYLENE GLYCOL (3,6,6-TRIMETHYL-2-PHENYLHEPTYN-4-DIOL-2,3)

E. D. Venus-Danilova and V. I. Serkova

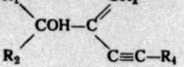
The study of the transformations of ditertiary $\alpha$-glycols (pinacols) of the acetylene series (I) on catalytic treatment with sulfuric acid [1-3] showed that this transformation depends on the nature of the radicals $R_1$, $R_2$, $R_3$, and $R_4$ and on their disposition relative to each other in the glycol molecule.



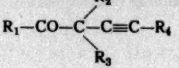
(I)

Up to the present time 11 glycols of this type, containing methyl and aryl radicals ($R_1$, $R_2$, and $R_3$) attached to the hydroxylated carbon atoms 1 and 2 and a phenyl or tert-butyl ($R_4$) in the acetylenic radical, have been studied.

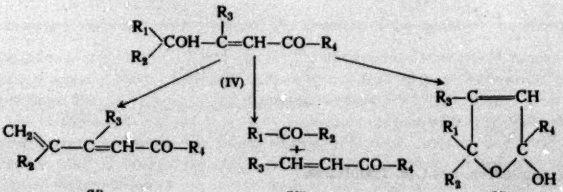
On heating with 20-46% sulfuric acid these glycols are transformed in three directions: 1) dehydration with formation of an enynic alcohol (II) [3] or decomposition products thereof [4]; 2) pinacoline rearrangement, as a result of which a ketone of the acetylene series (III) is obtained [5-9]; 3) isomerization of the glycol by a rearrangement of the acetylene-allene type with formation of an ethylenic $\gamma$-keto alcohol (IV) [10], for which further transformations are possible – formation of a dienic ketone (V) [11, 7], formation of products of the ketonic cleavage of the $\gamma$-keto alcohol (VI) [6, 8, 9], and cyclization of the $\gamma$-keto alcohol to form a substituted 2-hydroxydihydrofuran-2,5 (VII) [12, 10, 13, 6].



(II)



(III)



(IV)

(V)

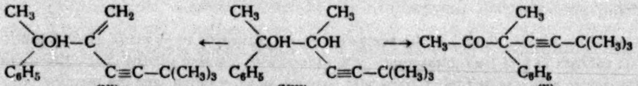
(VI)

(VII)

Any one transformation of acetylenic pinacols on treatment with sulfuric acid, for instance, the formation only of an acetylenic ketone [5], dehydration only [3, 4], or the formation only of a substituted hydroxydihydrofuran [13], was observed quite rarely. Usually the reaction goes in two or three directions with formation of various substances, but with one of them predominating.

It is noted that the dehydration of α-glycols (I) takes place in the presence of a methyl group on the second hydroxylated carbon atom ($R_3 = CH_3$) [3, 4], and the pinacoline rearrangement is facilitated by the presence of one or two phenyls on the first hydroxylated carbon atom ($R_1 = C_6H_5$ or $R_1 = R_2 = C_6H_5$) [5-7]. The isomerization of the glycol to an unsaturated γ-keto alcohol or products of the further transformation of the latter was observed to a greater or lesser degree with all the ditertiary α-glycols of the acetylene series, in the molecules of which there was an aryl radical on the second hydroxylated carbon atom ($R_3$ = aryl), regardless of the nature of the remaining radicals [6-10, 12, 13].

At present it is still impossible to predict accurately the direction of the transformations of pinacols of the acetylene series, since every radical occupying a definite position in the pinacol molecule influences its transformation. We observe only the total effect of these influences. However, the results obtained by us in the study of the transformations of sym. dimethylphenyl(phenylethynyl)ethylene glycol [4], unsym. methyldiphenyl-(tert-butylethynyl)ethylene glycol [3], unsym. methyldiphenyl(phenylethynyl)ethylene glycol [5], and trimethyl-(phenylethynyl)ethylene glycol [8], of which the first two gave only enynic alcohols and the last two gave ketones of the acetylene series, make a certain degree of foresight possible. It may be expected that on treatment with sulfuric acid sym. dimethylphenyl-(tert-butylethynyl)ethylene glycol (VIII) will be transformed either into an enynic alcohol (IX) or into a ketone of the acetylene series (X).



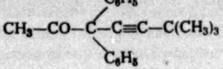
(IX) (VIII) (X)

$$\underset{\text{(IX)}}{CH_3(C_6H_5)C(OH)-C(=CH_2)-C\equiv C-C(CH_3)_3} \longleftarrow \underset{\text{(VIII)}}{CH_3(C_6H_5)C(OH)-C(OH)(CH_3)-C\equiv C-C(CH_3)_3} \longrightarrow \underset{\text{(X)}}{CH_3-CO-C(CH_3)(C_6H_5)-C\equiv C-C(CH_3)_3}$$

In order to test this hypothesis we synthesized sym. dimethylphenyl-(tert-butylethynyl)ethylene glycol (VIII) and studied its transformation on heating with 30% sulfuric acid.

Methylphenylacetylcarbinol and tert-butylacetylene were used for the preparation of the glycol by the method of Zh. I. Iotsich. The structure of the glycol was confirmed by oxidation with lead tetraacetate [14].

The only product of transformation of this glycol under the influence of sulfuric acid proved to be a ketone of the acetylene series – unsym. methylphenyl-(tert-butylethynyl) acetone (3,6,6-trimethyl-3-phenylheptyn-4-one-2 (X), which readily formed a semicarbazone and a 2,4-dinitrophenylhydrazone. The structure of the ketone was proved by oxidation, by its infrared spectrum, and by comparison of its ultraviolet spectrum with the corresponding spectrum of unsym. diphenyl-(tert-butylethynyl)acetone (XI)* (Figure 1).



$$CH_3-CO-C(C_6H_5)_2-C\equiv C-C(CH_3)_3$$

(XI)

## EXPERIMENTAL

### Sym. Dimethylphenyl-(tert-butylethynyl)ethylene Glycol (3,6,6-trimethyl-2-phenylheptyn-4-diol-2,3) (VIII).

Synthesis of the glycol. To an ethereal solution of ethylmagnesium bromide, prepared in the usual way was added an ethereal solution of tert-butylacetylene (b.p. 38-39.5°) taken in 50% excess. Toward the end of the reaction, the reaction mass was warmed (water-bath temperature 38-40°) until the evolution of ethane was complete. Methylphenylacetylcarbinol (b.p. 122-123° at 8 mm) dissolved in absolute ether, was slowly added to the organomagnesium compound of tert-butylacetylene, the latter being cooled with ice, and vigorously stirred.. After three days the organomagnesium complex was decomposed, and the reaction product was extracted with ether and dried with sodium sulfate. After the ether was distilled off, the residual mass quickly crystallized. By recrystallization from petroleum ether there was isolated a finely crystalline, colorless substance with m.p. 84-85°, which gave a positive reaction for the hydroxyl group (with methylmagnesium iodide), and also decolorized an aqueous solution of potassium permanganate and a solution of bromine in chloroform.

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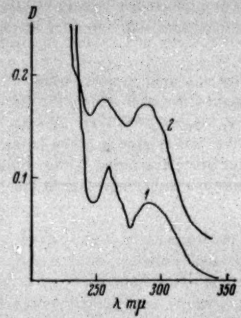
* This ketone was given to us by L. A. Pavlova, for which we express to her our thanks.



Ultraviolet spectra. 1) Unsym. methylphenyl-(tert-butylethynyl)acetone (X); 2) unsym. diphenyl-(tert-butylethynyl) acetone (XI).

The average yield of the glycol from three experiments amounted to 70%, calculated on the basis of the methylphenylacetylcarbinol taken.

Found %: C 77.94, 77.88; H 9.16, 8.98. Number of hydroxyl groups 2.1. M 247. $C_{16}H_{22}O_2$. Calculated %: C 78.04; H 8.94. Number of hydroxyl groups 2. M 246.

On the basis of the analytical data and properties, the substance with m.p. 84-85° should be regarded as 3,6,6-trimethyl-2-phenylheptyn-4-diol-2,3.

Oxidation of the glycol. To 5 g of the acetylenic glycol, dissolved in 50 ml of glacial acetic acid, was added in small portions 11 g of lead tetraacetate (20% excess) with vigorous stirring [14]. The mixture was heated for 3 hours, the acetic acid was half neutralized with aqueous potash solution, and the reaction products were steam distilled. Three fractions of the distillate were taken; from each one separately an ether extract was made which was washed with potash solution until a neutral reaction was obtained and dried with sodium sulfate. After the ether was distilled off from all three fractions, liquid products were obtained which gave a qualitative reaction for the carbonyl group. The material of the first fraction – a light-yellow liquid – formed a precipitate with 2,4-dinitrophenylhydrazine, which was not fully soluble in boiling ethyl alcohol. The boiling alcoholic solution was cooled, and from it light-yellow crystals with m.p. 164° were isolated, which gave no melting-point depression with known methyl tert-butylethynyl ketone 2,4-dinitrophenylhydrazone.

Found %: C 55.04; H 5.48; N 17.73. $C_{14}H_{16}O_4H_4$. Calculated %: C 55.26; H 5.26; N 18.41.

The infrared spectrum of the material of the first fraction indicates that there are a triple bond and a carbonyl group in the molecule of this substance, which fact also confirms the presence of methyl tert-butylethynyl ketone.

The residue insoluble in boiling ethyl alcohol on recrystallization of methyl tert-butylethynyl ketone 2,4-dinitrophenylhydrazone (m.p. 164°) was dissolved in glacial acetic acid on heating. In this case there were obtained red crystals with m.p. 248°. A mixture test with known acetophenone 2,4-dinitrophenylhydrazone (m.p. 249°) showed no melting-point depression. The semicarbazone with m.p. 198° also corresponded to acetophenone.

Thus the oxidation products of the acetylenic glycol (acetophenone and methyl tert-butylethynyl ketone) confirmed the hypothesis that the acetylenic glycol has the structure of sym. dimethylphenyl-(tert-butylethynyl) ethylene glycol.

### Unsym. Methylphenyl-(tert-butylethynyl)acetone (3,6,6-trimethyl-3-phenylheptyn-4-one-2) (X).

Action of 30% sulfuric acid on sym.dimethylphenyl-(tert-butylethynyl)ethylene glycol. Seven g of the glycol (mp. 84-85°) was gently boiled with a 10-fold quantity of sulfuric acid for 3 hours. The glycol melted, and the liquid gradually assumed a greenish-yellow hue, but neither resin formation nor fluorescence was observed. The ether extract from the acid solution was washed with dilute aqueous soda solution and dried with sodium sulfate. No products were isolated from the ether extract of the neutralized solution.

After the ether was eliminated from the extract of the acid solution, the light-yellow liquid obtained gave no reaction for the hydroxyl group, decolorized a solution of bromine in chloroform and aqueous potassium permanganate solution, and reacted with 2,4-dinitrophenylhydrazine and a solution of semicarbazide.

B.p. 100-101° (3 mm), $d_{20}^{20}$ 0.9258, $d_4^{20}$ 0.9242, $n_D^{20}$ 1.4993, $MR_D$ 72.47. $C_{16}H_{20}OF_3F$. . Calculated 70.49.

Found %: C 84.27, 84.04; H 8.85, 8.88. M 227. $C_{16}H_{20}O$. Calculated %: C 84.21; H 8.77. M 228.

The yellow 2,4-dinitrophenylhydrazone was obtained under the usual conditions [15]. M. p. 121° (from alcohol).

Found %: C 64.80, 64.60; H 5.98, 6.01; N 13.56, 13.43. $C_{22}H_{24}O_4N_4$. Calculated %: C 71.57; H 8.08; N 14.73.

After recrystallization (from alcohol) the semicarbazone melted at 214°.

Found %: C 71.58, 71.68; H 7.94; N 15.03, 14.81. $C_{17}H_{23}ON_3$. Calculated %: C 71.57; H 8.08; N 14.73.

Oxidation of the ketone (b.p. 100-101° at 3 mm). For 3 g of the ketone, 6.9 g of potassium permanganate was taken (calculated on the basis of 5 atoms of oxygen per ketone molecule). To a solution of the ketone in 25 ml of pyridine, 250 ml of 2% aqueous potassium permanganate solution was added at once. The oxidation was carried out with vigorous agitation at room temperature. After the solution was decolorized, the remaining 1.9 g of oxidizing agent was added in small portions until decolorization of the solution ceased. The oxidation continued for 7 hours. When the oxidation was finished, the manganese dioxide was filtered out from the clear solution, washed 3 times with small portions of hot water and treated with ether. After removal of ether there remained about 0.3 g of the original ketone, which was characterized by the 2,4-dinitrophenylhydrazone, b.p. 120°.

The pyridine and neutral oxidation products volatile with steam were distilled off from the filtrate at a low rate on heating. In the distillation the pyridine was converted to the salt by the calculated quantity of dilute sulfuric acid, after which an ether extract was made; from the latter there was isolated acetophenone, characterized by the semicarbazone (m.p. 198°) and the 2,4-dinitrophenylhydrazone (m.p. 247°) (mixture tests). Neutral oxidation products not volatile with steam were not found.

After the salts of the organic acids were concentrated and cautiously composed with dilute sulfuric acid, an oily substance was isolated from them, which was extracted with ether. After evaporation of the ether, water was added to the oily residue and the mixture was boiled; the volatile organic acids were then separated by steam distillation. From the three distillates obtained, stable silver salts were isolated by boiling with freshly precipitated silver carbonate. The silver content in these salts was determined after fractional recrystallization.

Found I distillate, 1st fraction %: Ag 51.81; I distillate, 3rd fraction %: Ag 53.91; III distillate, 1st fraction %: Ag 62.05, III distillate, 2nd fraction %: Ag 64.42. $CH_3COOAg$. Calculated %: Ag 64.65. $(CH_3)_3COOAg$; %: Ag 51.67.

After the acids volatile with steam were distilled off, there was extracted with ether a very insignificant quantity of a very impure solid substance with a sharply acid reaction, which vigorously decolorized aqueous potassium permanganate solution, and which was not further investigated.

The formation of acetophenone, acetic acid, and trimethylacetic acid on oxidation of ketone (X) (b.p. 100-101° at 3 mm) confirms the formula proposed for the ketone.

When a smaller amount of the oxidizing agent was used (4 atoms of oxygen per ketone molecule), trimethylpyruvic acid was also found among the acid products; it was isolated from the acidmixture in the form of the rapidly precipitated, yellow 2,4-dinitrophenylhydrazone, m.p. 174° after recrystallization from alcohol. A mixture test with the 2,4-dinitrophenylhydrazone (m.p. 174°) obtained from specially synthesized trimethylpyruvic acid [16] showed no melting-point depression.

Found %: C 46.14; H 4.48; N 18.20, 18.30. $C_{12}H_{14}O_6N_4$. Calculated %: C 46.16; H 4.49; N 18.06.

Spectra of unsym. methylphenyl-(tert-butylethynyl)acetone (X). The ultraviolet spectrum was taken in ethyl alcohol with an SF-4 spectrophotometer. For comparison the spectrum of unsym. diphenyl-(tert-butylethynyl)acetone (X) was also obtained under similar conditions. The obvious similarity of the absorption curves for the two ketones may be seen in the figure. The maxima and minima correspond to the same wavelengths: (X) – $\lambda_{max}$ 260 mμ ε 560; $\lambda_{max}$ 296 mμ, ε 375. (XI) – $\lambda_{max}$ 258 mμ, ε 890; $\lambda_{max}$ 290 mμ, ε 870.

The infrared spectrum of unsym. methylphenyl-(tert-butylethynyl)-acetone (X) was taken with an IKS-12 single-beam spectrometer provided with LiF and NaCl prisms, as well as an F-1 glass prism. The spectrum showed that ketone (X) contains an unconjugated carbonyl group (1724 $cm^{-1}$) and an acetylenic bond (2224 $cm^{-1}$). Bands of the monosubstituted benzene nucleus (1600, 1498, 705 $cm^{-1}$) and apparently the $(CH_3)_3C$– group (1277 $cm^{-1}$) are also present in the spectrum. The characteristic frequencies of the $CH_2$ group – 6100 and 810 $cm^{-1}$ – are absent in the spectrum.

The infrared spectra were taken by T. V. Iakovleva and the analyses were carried out by L. A. Maretina, for which we express to them our thanks.

## SUMMARY

1. Sym. dimethylphenyl-(tert-butylethynyl)ethylene glycol (3,6,6-trimethyl-2-phenylheptyn-4-diol-2,3), not described in the literature, has been synthesized.

2. It has been shown that on heating with 30% sulfuric acid the glycol is converted to a ketone of the acetylene series – unsym. methylphenyl-(tert-butylethynyl)acetone (3,6,6-trimethyl-3-phenylheptyn-4-one-2).

## LITERATURE CITED

[1] E. D. Venus-Danilova, L. A. Pavlova, V. I. Serkova, and E. P. Brichko, Wks. LTI, No. 30,38 (1954).

[2] E. D. Venus-Danilova, L. A. Pavlova, and A. Fabritsy Herald Leningrad State Univ. 16, No. 3, 117 (1956).

[3] E. D. Venus-Danilova, V. I. Serkova, and A. V. El'tsov, J. Gen. Chem. 27, 334 (1957).*

[4] E. D. Venus-Danilova and V. I. Serkova, J. Gen. Chem. 24, 998 (1954).*

[5] E. D. Venus-Danilova, E. P. Brichko, and L. A. Pavlova, J. Gen. Chem. 19, 951 (1949).*

[6] E. D. Venus-Danilova and L. A. Pavlova, J. Gen. Chem. 19, 1755 (1949).*

[7] E. D. Venus-Danilova and L. A. Pavlova, J. Gen. Chem. 20, 82 (1950).*

[8] E. D. Venus-Danilova, V. I. Serkova, and L. A. Pavlova, J. Gen. Chem. 21, 2210 (1951).*

[9] E. D. Venus-Danilova and V. I. Serkova, J. Gen. Chem. 22, 1563 (1952).*

[10] E. D. Venus-Danilova and E. P. Brichko, J. Gen. Chem. 17, 1549 (1947).

[11] E. D. Venus-Danilova and A. Fabritsy, J. Gen. Chem. 26, 892 (1956).*

[12] A. E. Favorskii and E. D. Venus, J. Russ. Chem. Soc. 47, 133 (1915).

[13] E. D. Venus-Danilova and E. P. Brichko, J. Gen. Chem. 17, 1849 (1957).*

[14] Criegee, Ber. 64, 260 (1931); coll., "New Methods of Preparative Organic Chemistry." IL, 150 (1950).**

[15] R. Shriner and R. Fuson. Systematic Qualitative Analysis of Organic Compounds. IL, 173 (1950).**

[16] Glucksmann, Monatsh, 10, 771 (1889).

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*See C. B. Translation

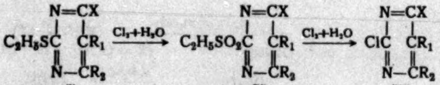
**Russian translation.

# INVESTIGATIONS IN THE PYRIMIDINE SERIES. ACTION OF HYDROGEN PEROXIDE ON MERCAPTOPYRIMIDINES. FORMATION OF PYRIMIDINE SULFONES AND THEIR INSTABILITY IN THE PRESENCE OF HYDROGEN PEROXIDE

Ch'ih Yueh-fon and Ch'en Shu-feng

It is known that 2-ethylthiopyrimidines (I, X = Cl, OR, or $NH_2$), on reaction with chlorine in an aqueous medium at 0°, form pyrimidine sulfones (II, X = Cl, OR, or $NH_2$), which can easily be isolated [1-5].

This reaction follows a peculiar course: on treatment with chlorine the unsaturation of the pyrimidine ring (I) is unchanged, while the alkylthio group is oxidized, as a result of which a stable alkanesulfonylpyrimidine (II) is formed.

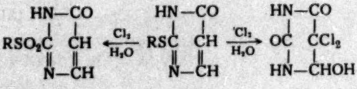


(I) (II) (III)

$R_1 = R_2 = H$;
$R_1 = Br$, $R_2 = H$;
$R_1 = C_2H_5$, $R_2 = CH_3$;

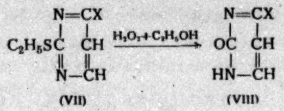
$R_1 = CH_3$, $R_2 = H$;
$R_1 = COOC_2H_5$, $R_2 = H$;
$R_1 = R_2 = CH_3$; $R_1 = C_3H_7$-n, $R_2 = CH_3$.

Treatment with chlorine at a somewhat elevated temperature may lead to replacement of the ethanesulfonyl group of pyrimidine (II) by chlorine [1] with formation of a pyrimidine derivative (III). Thus 2-ethylthio-4-chloro-5-carboethoxypyrimidine (I, $R_1 = COOC_2H_5$, $R_2$ = H, X = Cl), on treatment with chlorine at 30-40°, was converted to 2,4-dichloro-5-carboethoxypyrimidine [1] (III, $R_1 = COOC_2H_5$, $R_2$ = H, X = Cl). At the beginning of the reaction, in this case, there was formed 2-ethanesulfonyl-4-chloro-5-carboethoxypyrimidine (II, $R_1 = COOC_2H_5$, $R_2$ = H, X = Cl), which by the further action of chlorine was converted to 2,4-dichloro-5-carboethoxypyrimidine (III, $R_1 = COOC_2H_5$, $R_2$ = H, X = Cl). Another case of replacement of the ethanesulfonyl group by chlorine was noted by Ch'ih and Ling. They found that 2-ethylthio-4-methoxy-5,6-dimethylpyrimidine (I, $R_1 = R_2 = CH_3$, X = $OCH_3$) on treatment with chlorine (at 0-15° in 90% aqueous methanol) gave 2-chloro-4-methoxy-5,6-dimethylpyrimidine (III, $R_1 = R_2 = CH_3$, X = $OCH_3$) and 2-ethanesulfonyl-5,6-dimethyl-4-methoxypyrimidine (II, $R_1 = R_2 = CH_3$, X = $OCH_3$) [4]. Johnson and Sprague [6] stated that 2-alkylthio-4-hydroxypyrimidines (IV) on treatment with chlorine water formed derivatives of 2,4-diketohexahydropyrimidine (V); 2-alkanesulfonyl-4-hydroxypyrimidines (VI) were not isolated in this case. This reaction may be represented in the following manner:

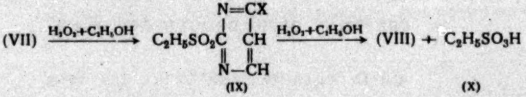


(VI) (IV) (V)

Ch'ih and Ch'en [7] found that on treatment of 2-ethylthiopyrimidines [VII, X = Cl $OCH_3$, $OC_2H_5$, $NH_2$, $NHCH_3$, or $N(C_2H_5)_2$] with hydrogen peroxide in ethanol, 2-hydroxypyrimidines [VIII, X = Cl, $OCH_3$, $OC_2H_5$, $NH_2$, $NHCH_3$, or $N(C_2H_5)_2$] are formed, as shown in the scheme


(VII) (VIII)

The authors proposed the following reaction mechanism:


(IX) (X)

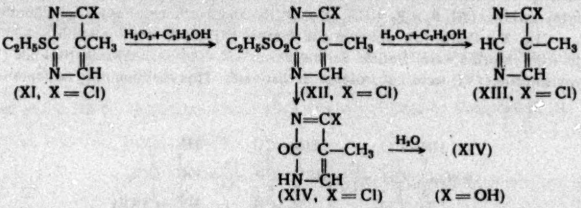
The proposed mechanism was experimentally supported by the fact that 2-ethanesulfonyl-4-chloropyrimidine [1] (IX, X = Cl), obtained by treatment of 2-ethylthio-4-chloropyrimidine with chlorine in water at 0°, reacts with hydrogen peroxide in ethyl alcohol to form 2-hydroxy-4-chloropyrimidine [7] (VIII, X = Cl). Ch'ih and Ch'en noted also that 2-ethylthio-4-alkoxypyrimidines (VII, X = $OCH_3$ or $OC_2H_5$) on reaction with hydrogen peroxide formed not only 2-hydroxy-4-alkoxypyrimidines (VIII, X = $OCH_3$ or $OC_2H_5$), but also uracil (VIII, X = = OH) [7]. The authors explained the formation of uracil as the result of the hydrolysis of 2-hydroxy-4-alkoxypyrimidines with the participation of ethanesulfonic acid (X) as catalyst:

$$\underset{(X=OCH_3 \text{ or } OC_2H_5)}{\text{(VII)}} \xrightarrow{H_2O_2+C_2H_5OH} \underset{(X=OCH_3 \text{ or } OC_2H_5)}{\text{(VIII)} + \text{(X)}}$$

$$\underset{(X=OCH_3 \text{ or } OC_2H_5)}{\text{(VIII)}} \xrightarrow[H_2O]{C_2H_5SO_3H} \underset{(X=OH)}{\text{(VIII)}}$$

In the present article the action of hydrogen peroxide on 2-ethylthio-5-methylpyrimidines [XI, X = Cl, $OCH_3$, $OC_2H_5$, $NH_2$, $NHCH_3$, or $N(C_2H_5)_2$] under various conditions is described in detail.

In the reaction of 2-ethylthio-4-chloro-5-methylpyrimidine (XI, X = Cl) with 30% hydrogen peroxide in ethyl alcohol, 2-ethanesulfonyl-4-chloro-5-methylpyrimidine (XII, X = Cl), 4-chloro-5-methylpyrimidine (XIII, X = Cl), and thymine (XIV, X = OH) were formed. 4-Chloro-5-methylpyrimidine, the formation of which was rather unexpected, may have been obtained from 2-ethanesulfonyl-4-chloro-5-methylpyrimidine reduction with hydrogen peroxide. The isolation of thymine may serve to confirm the hypothesis that 2-hydroxy-4-chloro-5-methylpyrimidine (XIV, X = Cl) occurs in the reaction products and is converted to thymine on recrystallization from dilute ethyl alcohol or water. The given conversions are shown below.


(XI, X = Cl) (XII, X = Cl) (XIII, X = Cl) (XIV, X = Cl) (X = OH)

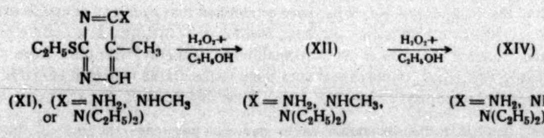
On treatment of a 2-ethylthio-4-alkoxy-5-methylpyrimidine (XI, X = $OCH_3$ or $OC_2H_5$) with 30% hydrogen peroxide in ethyl alcohol, there were obtained a 2-ethanesulfonyl-4-alkoxy-5-methylpyrimidine (XII, X = $OCH_3$

or $OC_2H_5$), a 2-hydroxy-4-alkoxy-5-methylpyrimidine, (XIV, X = $OCH_3$ or $OC_2H_5$), and thymine (XIV, X = OH). Apparently the pyrimidine sulfone, formed at the beginning of the reaction, reacted further with hydrogen peroxide to form a 2-hydroxy-4-alkoxy-5-methylpyrimidine (XIV, X = $OCH_3$ or $OC_2H_5$), which then was converted to thymine (XIV, X = OH) by the catalytic effect of ethanesulfonic acid also formed in the reaction. The scheme given below indicates the course of this reaction.

$$\underset{(X=OCH_3 \text{ or } OC_2H_5)}{(XI)} \xrightarrow{H_2O_2+C_2H_5OH} \underset{(X=OCH_3 \text{ or } OC_2H_5)}{(XII)} \xrightarrow{H_2O_2+C_2H_5OH} \underset{(X=OCH_3 \text{ or } OC_2H_5)}{(XIV)} + (X)$$

$$\underset{(X=OCH_3 \text{ or } OC_2H_5)}{(XIV)} \xrightarrow[H_2O]{C_2H_5SO_3H} \underset{(X=OH)}{(XIV)}$$

2-Ethylthio-4-amino-5-methylpyrimidine and its alkylamino derivatives [XI, X = $NH_2$, $NHCH_3$, or $N(C_2H_5)_2$] reacted with 30% hydrogen peroxide in ethyl alcohol to form 2-ethanesulfonyl-4-amino-5-methylpyrimidine and its alkylamino derivatives [XII, X = $NH_2$, $NHCH_3$, $N(C_2H_5)_2$], and 2-hydroxy-4-amino-5-methylpyrimidine and its alkylamino derivatives [XIV, X = $NH_2$, $NHCH_3$, or $N(C_2H_5)_2$]. The 2-ethanesulfonyl group in amino- and alkylaminopyrimidine sulfones [XII, X = $NH_2$, $NHCH_3$, or $N(C_2H_5)_2$] on treatment with hydrogen peroxide was easily replaced by a hydroxy group, whereupon 2-hydroxy-4-amino-5-methylpyrimidine or N-alkylaminopyrimidines [XIV, X = $NH_2$, $NHCH_3$, or $N(C_2H_5)_2$] were formed. These conversions are indicated by by the scheme


N=CX
C₂H₅SC C–CH₃
N–CH
H₂O₂+ C₂H₅OH
(XII)
H₂O₂+ C₂H₅OH
(XIV)
(XI), (X = NH₂, NHCH₃ or N(C₂H₅)₂)
(X = NH₂, NHCH₃, N(C₂H₅)₂)
(X = NH₂, NHCH₃, N(C₂H₅)₂)

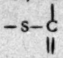
It is of interest to note that on treatment of 2-ethylthiopyrimidines [7] [VII, X = Cl, $OCH_3$, $OC_2H_5$, $NH_2$, $NHCH_3$, or $N(C_2H_5)_2$] with 30% hydrogen peroxide, pyrimidine sulfones were not isolated, while 2-ethylthio-5-methylpyrimidines [XI, X = Cl, $OCH_3$, $OC_2H_5$, $NH_2$, $NHCH_3$, or $N(C_2H_5)_2$] under the same conditions form pyrimidine sulfones in varying yields. Apparently, in the presence of a $CH_3$ group in position 5 of the pyrimidine ring, the rate of oxidation of 2-ethylthiopyrimidines by hydrogen peroxide decreases, and in this case the oxidation may stop at the pyrimidine sulfone [XII, X = Cl, $OCH_3$, $OC_2H_5$, $NH_2$, $NHCH_3$, or $N(C_2H_5)_2$] stage.

We decided also to conduct several experiments showing the dependence of the yield of pyrimidine sulfones [XII, X = Cl, $OCH_3$, $OC_2H_5$, $NH_2$, $NHCH_3$, or $N(C_2H_5)_2$] on the hydrogen peroxide concentration and the relation between the hydrogen peroxide concentration and the rate of replacement of the 2-ethanesulfonyl group in pyrimidine sulfones [XII, X = Cl, $OCH_3$, $OC_2H_5$, $NH_2$, $NHCH_3$, or $N(C_2H_5)_2$]. The results of these experiments are shown in Tables 1, 2, and 3.

It has been established that 2-ethylthio-4-chloro-5-methylpyrimidine (XI, X = Cl) on reaction with hydrogen peroxide forms 2-ethanesulfonyl-4-chloro-5-methylpyrimidine (XII, X = Cl) in various yields depending on the hydrogen peroxide concentration. When the latter was 17.5%, the yield of pure pyrimidine sulfone (XII, X = Cl) amounted to 82.5%; no by-products were isolated in this case. If the hydrogen peroxide concentration is gradually decreased, the yield of pyrimidine sulfone also gradually decreases, and the amount of original alkylthiopyrimidine (XI, X = Cl) in the reaction products increases. With 3% hydrogen peroxide the yield of pyrimidine sulfone was 25.3%, and the recovery of original alkylthiopyrimidine (XI, X = Cl) amounted to 70%. The use of hydrogen peroxide having a concentration greater than 17.5% leads to a decrease in the yield of pyrimidine sulfone (XII, X = Cl). With 20% hydrogen peroxide, 4-chloro-5-methylpyrimidine (XIII, X = Cl) was isolated from the reaction products in 20% yield. With 24.8% hydrogen peroxide another reaction product was obtained – thymine (XIV, X = OH) – in 52% yield. With 36% hydrogen peroxide, 4-chloro-5-methylpyrimidine (XIII, X = Cl) was isolated in 24% yield and thymine in 75% yield; no pyrimidine sulfone was obtained in this experiment.

2-Ethylthio-4-ethoxy-5-methylpyrimidine (XI, X = $OC_2H_5$) on treatment with hydrogen peroxide gave 2-ethanesulfonyl-4-ethoxy-5-methylpyrimidine (XII, X = $OC_2H_5$); the yield of which also depended on the hydrogen peroxide concentration. With 16.5% hydrogen peroxide the pyrimidine sulfone (XII, X = $OC_2H_5$) was obtained in 78.5% yield, while the quantity of recovered original alkylthiopyrimidine (XI, X = $OC_2H_5$) amounted to 15%. As the hydrogen peroxide concentration was decreased, the yield of pyrimidine sulfone fell, and the recovery of original alkylthiopyrimidine increased (XI, X = $OC_2H_5$). The yield of pyrimidine sulfone also decreased with increase in the hydrogen peroxide concentration. On treatment with 17.5% hydrogen peroxide the reaction involved the 2-methanesulfonyl group of the pyrimidine sulfone, as a result of which 2-hydroxy-4-ethoxy-5-methylpyrimidine (XIV, X = $OC_2H_5$) was obtained in 15% yield. With 21.5% hydrogen peroxide, thymine was found in 10.7% yield in the reaction products. On treatment with 36% hydrogen peroxide, 2-hydroxy-4-ethoxy-5-methylpyrimidine was obtained in 30% yield and thymine in 65.5% yield, while the pyrimidine sulfone was not obtained.

The yield of 2-ethanesulfonyl-4-amino-5-methylpyrimidine (XII, X = $NH_2$), formed on treatment of 2-ethylthio-4-amino-5-methylpyrimidine (XI, X = $NH_2$) with hydrogen peroxide, also varied in dependence on the hydrogen peroxide concentration. In experiments with 20% hydrogen peroxide the yield of pyrimidine sulfone (XII, X = $NH_2$) was 85.7%, while the recovery of original alkylthiopyrimidine (XI, X = $NH_2$) amounted to 8%. As the hydrogen peroxide concentration decreased, the yield of pyrimidine sulfone sharply fell, and the recovery of original alkylthiopyrimidine (XI, X = $NH_2$) rose. The yield of pyrimidine sulfone also decreased with increase in the hydrogen peroxide concentration, while the yield of 2-hydroxy-4-amino-5-methylpyrimidine was obtained in 18% yield. With 36% hydrogen peroxide the yield of 2-hydroxy-4-amino-5-methylpyrimidine was 85.6%; the pyrimidine sulfone was not obtained in this case.

Thus, as a result of the work carried out, it has been established that hydrogen peroxide oxidizes 2-alkylthio-5-methylpyrimidines [XI, X = Cl, $OCH_3$, $OC_2H_5$, $NH_2$, $NHCH_3$, or $N(C_2H_5)_2$]. At a certain hydrogen peroxide concentration the oxidation may stop at the 2-alkanesulfonyl-5-methylpyrimidine stage [XII, X = Cl, $OCH_3$, $OC_2H_5$, $NH_2$, $NHCH_3$, $N(C_2H_5)_2$]. On treatment with more concentrated hydrogen peroxide the 2-alkanesulfonyl group was replaced by a hydroxyl group; i. e., pyrimidine sulfones [XII, X = Cl, $OCH_3$, $OC_2H_5$, $NH_2$, $NHCH_3$, $N(C_2H_5)_2$] proved unstable in the presence of excess hydrogen peroxide; the  $-\mathrm{S}-\overset{|}{\underset{\|}{\mathrm{C}}}$ bond was easily broken.

Derivatives of uracil, thymine, and cytosine are often found among the products of metabolism. Organic peroxides are usually present in biological systems. It may be assumedthat similar intermolecular oxidation-reduction occurs in biological systems. Alkylthiopyrimidines and pyrimidine sulfones can scarcely be present in biological systems.

In the future the authors intend to study the action of organic peroxides on alkylthiopyrimidines.

## EXPERIMENTAL

### Syntheses of Alkylthiopyrimidines

**2-Ethylthio-4-hydroxy-5-methylpyrimidine (XI, X = OH)** was prepared thru the condensation of the sodium derivative of ethyl $\alpha$-formylpropionate with ethyl pseudothiourea hydrobromide according to the directions of Wheeler and Johnson [8]. A yellowish, crystalline substance with m.p. 154-155° (from water) was obtained. The sodium derivative of the ethyl $\alpha$-formylpropionate was synthesized according to the directions of Harkins and Johnson [9].

**2-Ethylthio-4-chloro-5-methylpyrimidine (XI, X = Cl)** was prepared according to the directions of Wheeler and Johnson [8]; b.p. 135° (14 mm).

**2-Ethylthio-4-methoxy-5-methylpyrimidine (XI, X = $OCH_3$).** 2-Ethylthio-4-chloro-5-methylpyrimidine (94.3 g, or 0.5 mole) was added with stirring to a cooled solution of sodium methoxide in methyl alcohol (0.5 mole with a slight excess in 200 ml of methyl alcohol), which was cooled to 5° beforehand. The mixture was left overnight. As much water was then added as was required for solution of the sodium chloride precipitate. The mixture was treated with ether, the ether extract was dried with anhydrous sodium sulfate and filtered, and the solvent was driven off. The substance obtained was purified by distillation in vacuo; b. p. 104-105° (4 mm). Yield, 85 g (92.4%).

Found %: N 15.15, 15.18. $C_8H_{12}ON_2S$. Calculated %: N 15.21.

2-Ethylthio-4-ethoxy-5-methylpyrimidine (XI, X = $OC_2H5$) was synthesized according to the directions of Sprague and Johnson [1]; b.p. 108° (3 mm).

2-Ethylthio-4-amino-5-methylpyrimidine (XI, X = $NH_2$) was prepared by the method of Wheeler and Johnson [8]; m.p. 96-97°.

2-Ethylthio-4-methylamino-5-methylpyrimidine (XI, X = $NHCH_3$). 2-Ethylthio-4-chloro-5-methylpyrimidine (9.43 g, or 0.05 mole) was added to 15 g of 33% aqueous methylamine solution. The mixture was heated in a sealed tube at 100° for 6 hours. After cooling, the reaction mass was a yellowish oil mixed with a certain amount of a solid substance crystallizing in the form of leaflets. The solid substance was filtered off. After complete removal of the solvent from the mother liquor in a vacuum desiccator, a solid substance was obtained. Both portions of the substance were combined and recrystallized from absolute ether. White leaflets with m.p. 58.5-60° were obtained. On standing in air for 2-3 hours the crystals deliquesced, changing to an oil.

Hydrochloride. As the crystals obtained above very readily deliquesced in air, the substance was heated with a small volume of alcoholic hydrochloric acid solution, after which the hydrochloride precipitated in the form of white leaflets. The hydrochloride was recrystallized from anhydrous alcohol; m.p. 228-229°. It did not deliquesce in air. Qualitative analysis showed the presence of sulfur, nitrogen, and chlorine.

Found %: N 19.08, 19.12; S 16.12, 16.26. $C_8H_{13}N_3S \cdot HCl$. Calculated %: N 19.5; S 16.14.

2-Ethylthio-4-diethylamino-5-methylpyrimidine [XI, X = $N(C_2H_5)_2$]. 2-Ethylthio-4-chloro-5-methylpyrimidine (9.43 g, or 0.05 mole) and diethylamine (10 ml, or 0.14 mole) were dissolved in 14 ml of ethyl alcohol. The mixture was heated to 100° for 6 hours. After cooling, the diethylaminopyrimidine separated in the form of leaflets; the solution was a viscous oil. The crystals were filtered off, and the viscous, oily liquid was evaporated in a vacuum desiccator. In the residue a yellowish, crystalline substance was obtained. The crystals were combined and recrystallized from anhydrous alcohol; m.p. 75-76°. On standing in air, the crystals quickly changed to an oil.

Hydrochloride. Since the substance quickly deliquesced in air, it was heated with alcoholic hydrochloric acid solution to obtain the corresponding hydrochloride. The white, crystalline hydrochloride, after recrystallization from ethyl alcohol, had m.p. 223-224°.

Found %: N 17.52, 16.64; Cl 13.96, 13.97. $C_{11}H_{19}N_3S \cdot HCl$. Calculated %: N 16.06; Cl 13.55.

## Action of Hydrogen Peroxide on Alkylthiopyrimidines

1 Action of hydrogen peroxide on 2-ethylthio-4-chloro-5-methylpyrimidine. Isolation of 2-ethanesulfonyl-4-chloro-5-methylpyrimidine (XII, X = Cl). 2-Ethylthio-4-chloro-5-methylpyrimidine (4 g, or 0.021 mole) was dissolved in 5 ml of ethyl alcohol. The solution was heated in a water bath. To the hot solution was added 5 ml of 30% hydrogen peroxide solution (0.044 mole). The violent reaction was finished within 20 minutes. On cooling the reaction mixture to room temperature a voluminous mass of white, crystalline material separated. The crystalline product was heated to boiling with ethyl acetate, and the undissolved material was filtered out from the hot solution (and saved for the following experiment). When the hot ethyl acetate solution was cooled, 2-ethanesulfonyl-4-chloro-5-methylpyrimidine separated out. The presence of nitrogen, chlorine, and sulfur in the compound was established by qualitative analysis. The substance melted at 65-66°. Sprague and Johnson [1] give m. p. 67.5-68°. A mixture of the obtained substance with the pyrimidine sulfone prepared according to the method of Sprague and Johnson [1] by treatment of 2-ethylthio-4-chloro-5-methylpyrimidine with chlorine and water showed no melting-point depression.

Found %: N 12.74, 12.71; S 14.51, 14.83; Cl 16.56, 16.60. $C_7H_9O_2N_2SCl$. Calculated %: N 12.70; S 14.53; Cl 16.07.

Isolation of 4-chloro-5-methylpyrimidine (XIII, X = Cl). The residue which had not dissolved in hot ethyl acetate was recrystallized from 50% ethyl alcohol. 4-Chloro-5-methylpyrimidine separated out in the form of white crystalline granules, m.p. 62-63°. The mother liquor was saved for the following experiment.

Found %: N 22.02, 21.78; Cl 27.88, 28.04. $C_5H_5N_2Cl$. Calculated %: N 21.80; Cl 27.59.

Isolation of thymine (XIV, X = OH). After 4 hours a white, crystalline substance separated out from the remaining mother liquor in the form of short needles with m.p. 321° (dec.). Fischer [10] and Johnson [11] give the same melting point.

Found %: N 22.22, 22.32. $C_5H_6O_2N_2$. Calculated %: N 22.23

2. Action of hydrogen peroxide on 2-ethylthio-4-methoxy-5-methylpyrimidine. Isolation of 2-ethanesulfonyl-4-methoxy-5-methylpyrimidine (XII, X = $OCH_3$). 2-Ethylthio-4-methoxy-5-methylpyrimidine (0.025 mole) was dissolved in 5 ml of ethyl alcohol, and the solution was heated in a water bath. To the hot solution was added a certain quantity of 30% hydrogen peroxide (0.05 mole). The white, crystalline substance which separated out as a result of the reaction was heated to boiling with ethyl formate and divided into a soluble and an insoluble fraction. 2-Ethanesulfonyl-4-methoxy-5-methylpyrimidine separated out from the ethyl formate solution; it was recrystallized from the same solvent. M.p. 67.5-68°.

Found %: N 12.88, 12.90; S 14.65, 14.77. $C_8H_{12}O_3N_2S$. Calculated %: N 12.96; S 14.83.

Isolation of 2-hydroxy-4-methoxy-5-methylpyrimidine (XIV, X = $OCH_3$). The insoluble fraction obtained above was heated to boiling with methyl alcohol and separated into 2-hydroxy-4-methoxy-5-methylpyrimidine and thymine (not purified). The first substance was recrystallized from methanol; it melted at 182-183°.

Found %: N 19.11, 19.32, $C_6H_8O_2N_2$. Calculated %: N 20.00.

The unpurified thymine was recrystallized from water. M.p. 321° (dec.).

3. Action of hydrogen peroxide on 2-ethylthio-3-ethoxy-5-methylpyrimidine. Isolation of 2-ethanesulfonyl-4-ethoxy-5-methylpyrimidine (XII, X = $OC_2H_5$). 2-Ethylthio-4-ethoxy-5-methylpyrimidine (0.025 mole) was heated in a water bath with a certain quantity of 30% hydrogen peroxide (0.05 mole) in 5 ml of ethyl alcohol. The white, crystalline substance formed in the reaction was heated to boiling with ethyl acetate and divided into a soluble and an insoluble fraction . 2-Ethanesulfonyl-4-ethoxy-5-methylpyrimidine separated out from the ethyl acetate solution; it was purified by recrystallization from the same solvent; m.p. 67-68°. Sprague and Johnson [1] give the same melting point.

Found %: S 12.90, 13.98. $C_9H_{14}O_3N_2S$. Calculated %: S 13.93.

The insoluble part was fractionated, recrystallized from water, and separated into two compounds – 2-hydroxy-4-ethoxy-5-methylpyrimidine and thymine. The 2-hydroxy-4-ethoxy-5-methylpyrimidine (XIV, X = $OC_2H_5$), after recrystallization from water, had m.p. 212-213°. Sprague and Johnson [2] give the same melting point.

Found %: N 18.08, 18.10. $C_7H_{10}O_2N_2$. Calculated %: N 18.18.

The thymine was recrystallized from water. M.p. 321° (dec.).

4. Action of hydrogen peroxide on 2-ethylthio-4-amino-5-methyl-pyrimidine. Isolation of 2-ethanesulfonyl-4-amino-5-methylpyrimidine (XII, X = $NH_2$). 2-Ethylthio-4-amino-5-methylpyrimidine (0.02 mole) was heated in a water bath with a certain quantity of 30% hydrogen peroxide (0.045 mole) in 3 ml of ethyl alcohol. The white, crystalline product which separated out as a result of the reaction was heated to boiling with ethyl acetate and divided into a soluble and an insoluble fraction. 2-Ethanesulfonyl-4-amino-5-methylpyrimidine, which separated out from the ethyl acetate solution, was recrystallized from the same solvent. M.p. 135-136.5°.

Found %: S 15.82, 15.86. $C_7H_{11}O_2N_3S$. Calculated %: S 15.94.

Isolation of 2-hydroxy-4-amino-5-methylpyrimidine hydrochloride. The insoluble fraction obtained above was heated with ethyl alcohol containing hydrogen chloride. 2-Hydroxy-4-amino-5-methylpyrimidine hydrochloride, m.p. 288-290° (dec.), separated out from the cooled solution. Wheeler and Johnson [8] give m.p. 288° (with effervescence). Sprague and Johnson [2] give m.p. 288-290°.

Found %: N 26.15, 26.22. $C_5H_7ON_3 \cdot HCl$. Calculated %: N 26.02.

5. Action of hydrogen peroxide on 2-ethylthio-4-methylamino-5-methylpyrimidine. Isolation of 2-ethanesulfonyl-4-methylamino-5-methylpyrimidine (XII, X = $NHCH_3$). 2-Ethylthio-4-methylamino-5-methylpyrimidine (0.02 mole) was heated to boiling in a water bath with a certain quantity of 30% hydrogen peroxide (0.045 mole) in 3 ml of ethyl alcohol. The white, crystalline product formed in the reaction was heated to boiling with ethyl acetate and divided into a soluble and an insoluble fraction. 2-Ethanesulfonyl-4-methylamino-5-methylpyrimidine separated out from the ethyl acetate; it was recrystallized from the same solvent. M. p. 138-140°.

Found %: N 19.44, 19.46; S 14.89, 14.92. $C_8H_{13}O_2N_3S$. Calculated %: N 19.53; S 14.90.

Isolation of 2-hydroxy-4-methylamino-5-methylpyrimidine (XIV, X = $NHCH_3$). The fraction which had not dissolved in ethyl acetate was dissolved in 80% ethyl alcohol; on cooling of the solution 2-hydroxy-4-methylamino-5-methylpyrimidine, m.p. 235°, separated out.

Found %: N 30.22, 30.32. $C_6H_9ON_3$. Calculated %: N 30.22.

6. Action of hydrogen peroxide on 2-ethylthio-4-diethylamino-5-methylpyrimidine Isolation of 2-ethanesulfonyl-4-diethylamino-5-methylpyrimidine [XII, X = $N(C_2H_5)_2$]. 2-Ethylthio-4-diethylamino-5-methylpyrimidine (0.02 mole) was heated in a water bath with a certain volume of 30% hydrogen peroxide (0.045 mole) in 3 ml of ethyl alcohol. The white, crystalline reaction product was heated to boiling with ethyl acetate and divided into a soluble and an insoluble fraction. 2-Ethanesulfonyl-4-diethylamino-5-methylpyrimidine separated out from the solution; it was recrystallized from the same solvent. M.p. 139-140°.

Found %: N 16.92, 16.95; S 12.94, 12.92. $C_{11}H_{19}O_2N_3S$. Calculated %: N 16.34; S 12.46.

TABLE 1

Dependence of the Action of Hydrogen Peroxide on 2-Ethylthio-4-chloro-5-methylpyrimidine on the Concentration of the Former

| Hydrogen peroxide concentration (in %) | Yield of reaction products (in %) | | | Recovery of original alkylthiopyrimidine (in %) |
|---|---|---|---|---|
| | 2-ethanesulfonyl-4-chloro-5-methylpyrimidine | 4-chloro-5-methylpyrimidine | thymine | |
| 3 | 25.3 | — | — | 70.0 |
| 10 | 38.5 | — | — | 58.0 |
| 15.5 | 60.0 | — | — | 25.5 |
| 17.5 | 82.5 | — | — | — |
| 20 | 70.5 | 20.0 | — | — |
| 23.6 | 64.5 | 25.5 | — | — |
| 24.8 | 30.4 | 15.0 | 52 | — |
| 30 | 26.0 | 16.4 | 53.5 | — |
| 36 | — | 24.0 | 75.0 | — |

Isolation of 2-hydroxy-4-diethylamino-5-methylpyrimidine [XIV, X = $N(C_2H_5)_2$]. The fraction insoluble in ethyl acetate was dissolved in 80% ethyl alcohol, from which 2-hydroxy-4-diethylamino-5-methylpyrimidine, m.p. 232°, separated out on cooling.

Found %: N 23.75, 23.79. $C_9H_{15}ON_3$. Calculated %: N 23.20.

### Dependence of the Action of Hydrogen Peroxide on Alkylthiopyrimidines on its Concentration

Reactions of 2-ethylthio-4-R-5-methylpyrimidines (R = Cl, $OC_2H_5$, $NH_2$) with hydrogen peroxide of various concentrations were carried out. It was established that the yield of pyrimidine sulfones and the recovery of the original pyrimidine derivatives also depended on the hydrogen peroxide concentration. The results obtained are given in Tables 1-3.

### TABLE 2

Dependence of the Action of Hydrogen Peroxide on 2-Ethylthio-4-ethoxy-5-methylpyrimidine on the Concentration of the Former

| Hydrogen peroxide concentration (in %) | Yield of reaction products (in %) | | | Recovery of original alkylthiopyrimidine (in %) |
|---|---|---|---|---|
| | 2-ethanesulfonyl-4-ethoxy-5-methylpyrimidine | 2-hydroxy-4-ethoxy-5-methylpyrimidine | thymine | |
| 3 | 22.4 | — | — | 75.0 |
| 10 | 40.2 | — | — | 50.4 |
| 15 | 56.6 | — | — | 30.0 |
| 16.5 | 78.5 | — | — | 15.0 |
| 17.5 | 70.0 | 15 | — | — |
| 21.5 | 60.2 | 12.0 | 10.7 | — |
| 26.4 | 28.8 | 19.2 | 50.5 | — |
| 30 | 25.0 | 20.2 | 50.0 | — |
| 36 | — | 30 | 65.5 | — |

### TABLE 3

Dependence of the Action of Hydrogen Peroxide on 2-Ethylthio-4-amino-5-methylpyrimidine on the Concentration of the Former

| Hydrogen peroxide concentration (in %) | Yield of reaction product (in %) | | Recovery of original alkylthiopyrimidine (in %) |
|---|---|---|---|
| | 2-ethanesulfonyl-4-amino-5-methylpyrimidine | 2-hydroxy-4-amino-5-methylpyrimidine | |
| 3 | 25 | — | 70 |
| 10 | 35.5 | — | 60 |
| 15 | 52.5 | — | 30 |
| 20 | 85.7 | — | 8 |
| 23.6 | 78 | 18 | — |
| 24.8 | 62 | 21.5 | — |
| 26.4 | 550 | 42.5 | — |
| 30 | 45.5 | 41 | — |
| 36 | — | 85.6 | — |

The analyses for nitrogen, given in the present work, were performed by Ch'ao Ch'a-lung, Wang Tien-jeng and Fang Weng-Ch'ai for which the authors sincerely thank them.

## SUMMARY

1. 2-Ethylthio-4-chloro-5-methylpyrimidine on treatment with 30% hydrogen peroxide in ethyl alcohol formed 2-ethanesulfonyl-4-chloro-5-methylpyrimidine, 4-chloro-5-methylpyrimidine, and 2-hydroxy-4-chloro-5-methylpyrimidine (which changed to thymine on recrystallization from water or dilute ethyl alcohol).

2. 2-Ethylthio-4-methoxy- (or -ethoxy-)5-methylpyrimidine on reaction with 30% hydrogen peroxide in ethyl alcohol gave 2-ethanesulfonyl-4-methoxy- (or -ethoxy-)5-methylpyrimidine, 2-hydroxy-4-methoxy- (or -ethoxy-)5-methylpyrimidine, and thymine.

3. 2-Ethylythio-4-amino-(-N-methylamino- or -N-diethylamino-)5-methypyrimidine reacted with 30% hydrogen peroxide in ethyl alcohol to form 2-ethanesulfonyl-4-amino- (N-methylamino- or -N-diethylamino-) 5-methylpyrimidine and 2-hydroxy-4-amino- (-N-methylamino- and -N-diethylamino-) 5-methylpyrimidine.

4. The rate of oxidation of a 2-ethylthiopyrimidine by hydrogen peroxide is decreased if there is a $CH_3$ group in position 5 of the pyrimidine ring. The oxidation may stop at an intermediate stage, and in these cases pyrimidine sulfones can be isolated.

5. The yield of pyrimidine sulfones varies in dependence on the hydrogen peroxide concentration. With 17.5% hydrogen peroxide the yield of 2-ethanesulfonyl-4-chloro-5-methylpyrimidine was 82.5% With 16.5% hydrogen peroxide the yield of 2-ethanesulfonyl-4-ethoxy-5-methylpyrimidine amounted to 78.5%. With 20% hydrogen peroxide the yield of 2-ethanesulfonyl-4-amino-5-methylpyrimidine was 85.7%.

## LITERATURE CITED

[1] J. M. Sprague and T. B. Johnson, J. Am. Chem. Soc., 57, 2252 (1935).

[2] J. M. Sprague, and T. B. Johnson, J. Am. Chem. Soc., 58 423 (1936).

[3] Chi Yuoh-fong and Ling Yuoh-chern, Acta Chim. Sinica, 20, 108 (1954).

[4] Chi Yuoh-fong and Ling Youh-chern, Acta Chim. Sinica, 21, 385 (1955).

[5] Chi Yuoh-fong and Ling Yuoh-chern, Acta Chim. Sinica, 22, 3 (1956).

[6] T. B. Johnson and J. M. Sprague, J. Am. Chem. Soc., 60, 1622 (1938).

[7] Chi Youh-fong and Chen Shu-fung. Acta Chim. Sinica 22, 194 (1956).

[8] H. L. Wheeler, and T. B. Johnson, Am. Chem. J., 31, 591 (1904).

[9] Henry H. Harkins, T. B Johnson, J Am. Chem. Soc., 51, 1237 (1929).

[10] E. Fischer and G. Roeder, Ber.c 34, 3758 (1901).

[11] T. B. Johnson, Am. Chem. J., 40, 29 (1908).

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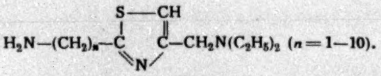
# INVESTIGATIONS IN THE THIAZOLE SERIES

## V. SYNTHESIS OF 2-δ-AMINO-n-BUTYL-4-N-DIETHYLAMINOMETHYLTHIAZOLE

Ch'ih Yueh-fon and Zin Shih-yung

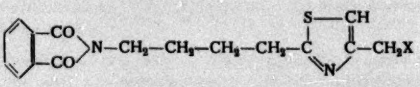
In previous papers [1, 2] we put forward a method of synthesizing 2-aminoalkyl-N-diethylaminomethylthiazole (I).



(I)

Similar alkylenediamines, containing a thiazole ring, may be active physiologically. S. G. Fridman [3] showed that N-β-dimethylaminoethyl-N-benzyl-2-amino-4-methylthiazole had an anthihystaminic effect. The introduction of a thiazole ring into β-phenylethylamine and its derivatives considerably lowers their toxicity [4, 5]. Goldberg (6) noted the antibacterial acitivity of 2-ω-aminoalkylthiazole derivatives. It was quite logical to consider that the toxicity of alkylenediamines would be reduced by the introduction of a thiazole ring.

In the present work we describe the synthesis of 2-δ-amino-n-butyl-4-N-diethylaminoethylthiazole (I, n = 4). The thioamide of δ-phthalimido-n-valeric acid was condensed with α, γ-dichloroacetone to form 2-δ-phthalimido-n-butyl-4-chloromethylthiazole (II, X = Cl), which was reacted with diethylamine to give 2-δ-phthalimido-n-butyl-4-N-diethylaminomethylthiazole (IIb, X = $N(C_2H_5)_2$).



(II)

(IIa), X = Cl;
(IIb), X = $N(C_2H_5)_2$.

The product obtained was treated with hydrazine hydrate by the method of Ing and Manske [7]. This removed the phthalyl group to give the required 2-δ-aminobutyl-4-N-diethylaminomethylthiazole (I, n = 4).

## EXPERIMENTAL

**δ-Bromovaleronitrile.** The 1,4-dibromobutane required for the synthesis was prepared from tetramethylene glycol by passing hydrogen bromide through it. The tetramethylene glycol was prepared by reducing diethyl succinate with sodium in ethyl alcohol. For the preparation of δ-bromovaleronitrile, 1,4-dibromobutane was treated with potassium cyanide by the method Goldberg and Kelly [8] described for the synthesis of γ-bromobutyronitrile.

1,4-Dibromobutane (65 g) was dissolved in 95 ml of ethyl alcohol and to the solution was added potassium cyanide solution (24 g of potassium cyanide in 48 ml of water) dropwise with heating and stirring. The addition of the potassium cyanide solution required about an hour and half and after this, the reaction mixture was heated and stirred for a further 1 hour. The cooled solution was poured into 240 ml of water and extracted 3 times with chloroform (45 ml portions). The chloroform extract was dried with anhydrous sodium sulfate and filtered, the solvent removed and the residual oil distilled in vacuum. The following fractions were collected: 1st b. p. 80-86° (4 mm), 14 g, unreacted 1,4-dibromobutane; 2nd b. p. 92-98° (4 mm), 12.5 g, (25.6%), δ-bromo-n-valeronitrile; 3rd b. p. 120-132° (4 mm), 4 g, 1,4-dicyanobutane.

δ-Phthalimido-n-valeronitrile. Potassium phthalimide (12 g) and δ-bromo-n-valeronitrile (9.5 g) were mixed with 35 ml of anhydrous ethyl alcohol and heated with stirring for 10 hours on an oil bath at 110-120° The solvent (about 20 ml) was partly evaporated and the residual liquid poured into 50 ml of water. The crystalline precipitate formed was recrystallized from ethyl alcohol. A fine, colorless powder with m. p. 74-76° was obtained. The yield of δ-phthalimido-n-valeronitrile was 8.1 g (60.5%).

Found %: N 12.18, 12.42. $C_{13}H_{12}O_2N_2$. Calculated %: N 12.28.

Thioamide of δ-phthalimido-n-valeric acid. Experiment 1. δ-Phthalimido-n-valeronitrile (1.2 g) was mixed with an alcohol solution of ammonium bisulfide (prepared by dissolving 3.0 g of $NH_3$ and 0.26 g of $H_2S$ in 7.2 ml of $C_2H_5OH$). The mixture was placed in a sealed tube, which was shaken periodically for 48 hours, and then the crystalline thioamide of δ-phthalimido-n-valeric acid with m. p. 145-146° was isolated. The yield was 34%.

Found %: N 10.19, 10.23; S 12.20. $C_{13}H_{12}O_2N_2S$. Calculated %: N 10.69; S 12.23.

Evaporation of the mother liquors and cooling yielded a compound with m.p. 217-218.5°, which contained nitrogen but no sulfur. It was assumed that this substance was δ-phthalimido-n-valeramide.

Found %: N 16.84, 16.61. $C_{13}H_{15}O_2N_3$. Calculated %: N 17.14.

Experiment 2. δ-Phthalimido-n-valeronitrile (10 g) was dissolved in 50 ml of anhydrous ethyl alcohol, to which was added tri-(β-ethanol)-amine (0.5 g). The solution was heated to 40° and a stream of dry hydrogen sulfide passed in for a period of 53 hours. On cooling, the solution yielded a crystalline substance with m. p. 112-120°. The yield of crude product was 7.8 g. The substance was purified by recrystallization from 50% ethyl alcohol. It crystallized in the form of a colorless finely crystalline powder with m.p. 142-144°. The yield of pure thioamide of δ-phthalimido-n-valeric acid was 5.8 g (50.5%).

Found %: N 10.28, 9.96; S 12.32. $C_{13}H_{14}O_2N_2S$. Calculated %: N 10.69; S 12.23.

2-δ-Phthalimido-n-butyl-4-chloromethylthiazole (II, X = Cl). δ-Phthalimido-n-valerothioamide (3.7 g) and α, γ-dichloroacetone (1.8 g) were mixed with 18 ml of anhydrous alcohol and heated for 3 hours. The solution was kept overnight in a refrigerator and then the colorless, crystalline substance with m.p. 78-81° was isolated. The yield of crude product was 2.3 g. The substance was purified by recrystallization from anhydrous ethyl alcohol. We obtained fine, microscopic crystals with m.p. 82-83°. The yield of pure 2-δ-phthalimido-n-butyl-4-chloromethylthiazole was 2.8 g (38.1%).

Found %: N 8.38, 9.03; S 10.14; Cl 10.02. $C_{16}H_{15}O_2N_2SCl$. Calculated %: N 8.37; S 9.58; Cl 10.59.

The mother liquor was concentrated under reduced pressure until the separation of a white, crystalline substance (m.p. 152-163°) began. The substance obtained, which was apparently the hydrochloride of 2-δ-phthalimido-n-butyl-4-chloromethylthiazole, dissolved in sodium bicarbonate with the evolution of $CO_2$. The solution obtained was extracted with chloroform. The extract was dried and the solvent distilled off. The sirupy residue was kept in ice overnight and yielded a small amount of a solid substance, which was recrystallized from ethyl alcohol to give microscopic crystals with m.p. 81-83°.

2-δ-Phthalimido-n-butyl-4-N-diethylaminomethylthiazole [II, X = $N(C_2H_5)_2$]. 2-δ-Phthalimido-n-butyl-4-chloromethylthiazole (1.5 g) and diethylamine (1.5 g) were dissolved in 50 ml of anhydrous ethyl alcohol. The solution was boiled for 6 hours. After removal of the ethyl alcohol, the residue was neutralized with soda solution and extracted three times with ethyl ether (5 ml of ethyl ether in each portion). The ether extract was dried with potash, filtered and the solvent distilled off. Attempts to purify the residual oil by distillation at a residual pressure of 100μ (bath temperature 300-310°) were unsuccessful.

For preparation of the hydrochloride, the crude 2-δ-phthalimido-n-butyl-4-N-diethylaminomethylthiazole was dissolved in a small volume of anhydrous ethanol and a 5% solution of hydrochloric acid in ethanol added dropwise until the pH of the solution equalled 4. Then ethyl ether was added to the alcohol solution dropwise until a slight turbidity appeared. The solution was kept in a refrigerator overnight, when it deposited fine, microscopic crystals, which were recrystallized from a mixture of alcohol and ether to form small leaves with m.p 105-106°.

Found %: N 9.87; S 7.38; Cl 8.41. $C_{20}H_{25}O_2N_3Cl \cdot HCl$. Calculated %: N 10.31; S 7.86; Cl 8.70.

2-δ-Amino-n-butyl-4-N-diethylaminomethylthiazole (I, n = 4). 2-δ-Phthalimido-n-butyl-4-N-diethylaminomethylthiazole (3.7 g) was dissolved in 80 ml of ethyl alcohol, to which was added 1 ml of hydrazine hydrate. The mixture was heated on a water bath under reflux for 1.5 hours. The ethyl alcohol was then removed under reduced pressure and the residual oil cooled and acidified with 6 N hydrochloric acid. The phthalyl hydrazide separated as a semisolid precipitate, which was filtered off. The filtrate was treated with 50 ml of 40% sodium hydroxide solution to liberate a yellow oil, which floated on the surface. To the oil, which had been separated from the aqueous solution, was added barium oxide (7 g) and the mixture heated for 1 hour on a water bath. After being cooled, the mixture was extracted three times with ether, using 20 ml portions of ether. The ether extracts were dried with anhydrous potash, filtered and the solvent evaporated. The residual oil was purified by vacuum distillation. The pure 2-δ-amino-n-butyl-4-N-diethylaminomethylthiazole boiled at 149-150° (6 mm). Yield was 0.9 g (37%).

Found %: N16.84, 17.07; S 12.93. $C_{12}H_{23}N_3S$. Calculated %: N 17.42; S 13.29.

The analyses given in this article were performed bv Ch'ao Ch'ang-ling, Wang Tieh-jeng, Ping Shu-k'uei, Wang We-ch'e, to whom the authors are extremely grateful.

## SUMMARY

1. The reaction of δ-bromo-n-valeronitrile with potassium phthalimide in ethyl alcohol lead to δ-phthalimido-n-valeronitrile, which was converted into δ-phthalimido-n-valerothioamide by reaction with ammonium bisulfide in ethyl alcohol and also by reaction with hydrogen sulfide in ethyl alcohol in the presence of tri-(β-ethanol)-amine.

2. δ-Phthalimido-n-valerothioamide was condensed with α, γ-dichloroacetone in ethyl alcohol to form 2-δ-phthalimido-n-butyl-4-chloromethylthiazole.

3. 2-δ-Phthalimido-n-butyl-4-chloromethylthiazole reacted with diethylamine to from 2-δ-phthalimido-n-butyl-4-N-diethylaminomethylthiazole and when this was heated with hydrazine hydrate, the phthalyl group was removed to yield the free amine—2-δ-amino-n-butyl-4-N-diethylaminomethylthiazole.

## LITERATURE CITED

[1] Chi Yuoh-Fong and Tshin Shi-Yuan, J. Am. Chem. Soc., 64, 90 (1942).

[2] Chi Yuoh-Fong and Tshin Shi-Yuan, Acta Chim. Sinica, 21, 401 (1955).

[3] S. G. Fridman, J. Gen. Chem. 23, 278 (1953). *

[4] W. S. Hinegardner and T. B. Johnson, J. Am. Chem. Soc., 52, 3724 (1930).

[5] W. S. Hinegardner, and T. B. Johnson, J. Am. Chem. Soc., 52, 4141 (1930).

[6] A. Goldberg and W. Kelly, J. Chem. Soc. 1947, 1371.

[7] H. R. Ing and R. H. Manske, J. Chem. Soc. 128, 2348 (1926).

[8] A. Goldberg and W. Kelly, J. Chem. Soc. 1947, 1369.

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*See C.B. Translation.

# AN ANOMALOUS REACTION OF α-HALO KETONES WITH ESTERS OF PHOSPHOROUS ACID

## VII. REACTIONS OF ESTERS OF PHOSPHOROUS ACID WITH CHLORINATED DERIVATIVES OF β-DIKETONES

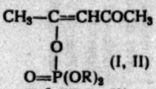
A. N. Pudovik and L. G. Biktimirova

Reactions of esters of phosphorous acid with brominated derivatives of some β-dicarbonyl compounds have been studied by B. A. Arbuzov and N. P. Bogonostseva [1]. These workers demonstrated that in the reaction of triethyl phosphite with dibenzoylbromomethane, tribenzoylbromomethane and bromoindanedione there are formed, respectively, dibenzoylmethane, tribenzoylmethane and indanedione. From the reaction with tribenzoylbromomethane, in addition to the tribenzoylmethane, there was isolated a fraction, the constants of which correspond to those of triethyl phosphate. The authors regard the radical mechanism of this reaction to be the most probable one: the free radicals of dibenzoylmethyl, tribenzoylmethyl and indanedionyl, which are formed in the first stage of the reaction, are later reduced either by hydrogens of triethyl phosphite or those of the solvent. Kreutzkamp and Kuser [2], who studied the reaction of trialkyl phosphites with chlorobenzoylacetone and tribenzoylchloromethane, also note the formation of only the products of reduction of the latter substances – benzoylacetone and tribenzoylmethane.

We have shown in a previous study [3] that α-bromo- and α-chloro-ketones, which possess a halogen atom on the primary carbon atom, behave differently in their reactions with phosphites. Bromo ketones react predominantly by the scheme of the Arbuzov rearrangement with formation of phosphonoketones, while chloroketones yield mainly the unsaturated phosphate esters. As was shown in one of our previous papers [4], the reactions of triethylphosphite and triisobutyl phosphite with chloro- and dichloro derivatives of acetylacetone and acetoacetic ester proceed completely anomalously with formation of unsaturated phosphate esters.

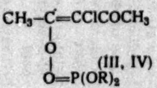
Continuing the development of these investigations, in the present work we studied the reactions of chloro- and dichloro-substituted derivatives of acetylacetone, benzoylacetone, dibenzoylmethane and dimedone (dimethylcyclohexanedione) with various phosphites. One might assume, in accord with the previously obtained results, that in all these reactions the unsaturated phosphate ester would form as either the intermediate or as the final products.

Reactions of chloro- and dichloroacetone with trimethyl phosphite and tri-n-butyl phosphite proceed completely anomalously: there were obtained, in yields of 60-80%, the corresponding 1-methyl-1-buten-3-onyl dialkyl or 1-methyl-2-chloro-1-buten-3-onyl dialkyl esters of phosphoric acid (see table, substances I-IV).



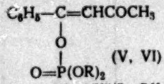
$$CH_3-\underset{\underset{\underset{O=P(OR)_2}{|}}{O}}{\overset{|}{C}}=CHCOCH_3 \quad (I, II)$$

(I) &(III) R=CH$_3$.



$$CH_3-\underset{\underset{\underset{O=P(OR)_2}{|}}{O}}{\overset{|}{C}}=CClCOCH_3 \quad (III, IV)$$

(II) & (IV) R=n-C$_4$H$_9$.

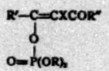


$$C_6H_5-\underset{\underset{\underset{O=P(OR)_2}{|}}{O}}{\overset{|}{C}}=CHCOCH_3 \quad (V, VI)$$

(V) R=CH$_3$; (VI) R=C$_2$H$_5$.

The presence of the double bond in these compounds was proved by bromination, according to McIlliney, while acetylacetone was obtained by careful hydrolysis of (I). It is interesting to note that compound (I) after

Constants of 1-Methyl-1-buten-3-onyl Dialkyl and 1-Methyl-2-chloro-1-buten-3-onyl Dialkyl Esters of Phosphoric Acid



$R'-\underset{\substack{|\\ O\\ |\\ O=P(OR)_2}}{C}=CXCOR''$

| | Names of compounds | Significance in the formula | | | | Boiling point (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ | | Content (in %) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | phosphorus | | chlorine | |
| | | R | R' | R'' | X | | | | found | calc. | found | calc. | found | calc. |
| (I) | 1-Methyl-1-buten-3-onyl dimethyl ester of phosphoric acid | $CH_3$ | $CH_3$ | $CH_3$ | H | 103—104° (2) | 1.2040 | 1.4572 | 46.00 | 46.06 | 14.40,<br>14.83 | 14.90 | — | — |
| (II) | 1-Methyl-1-buten-3-onyl di-n-butyl ester of phosphoric acid | n -$C_4H_9$ | $CH_3$ | $CH_3$ | H | 125—127 (1) | 1.0503 | 1.4510 | 74.86 | 73.77 | 10.64,<br>10.64 | 10.61 | — | — |
| (III) | 2-Chloro-1-methyl-1-buten-3-onyl dimethyl ester of phosphoric acid | $CH_3$ | $CH_3$ | $CH_3$ | Cl | 115 (2) | 1.3085 | 1.4710 | 51.79 | 50.93 | 12.71,<br>12.53 | 12.781 | 15.38 | 14.64 |
| (IV) | 2-Chloro-1-methyl-1-buten-3-onyl di-n-butyl ester of phosphoric acid | n -$C_4H_9$ | $CH_3$ | $CH_3$ | Cl | 138—139 (2) | 2.1202 | 1.4615 | 79.66 | 78.64 | 9.56,<br>9.91 | 9.49 | 11.31 | 10.87 |
| (V) | 1-Phenyl-1-buten-3-onyl dimethyl ester of phosphoric acid | $CH_3$ | $C_6H_5$ | $CH_3$ | H | 138—139 (1) | 1.2278 | 1.5262 | 67.52 | 65.55 | 11.68,<br>12.02 | 11.48 | — | — |
| (VI) | 1-Phenyl-1-buten-3-onyl diethyl ester of phosphoric acid | $C_2H_5$ | $C_6H_5$ | $CH_3$ | H | 170—172 (2) | 1.1611 | 1.5135 | 77.20 | 74.78 | 10.11 | 10.40 | — | — |
| (VII) | 2-Chloro-1-phenyl-1-buten-3-onyl dimethyl ester of phosphoric acid | $CH_3$ | $C_6H_5$ | $CH_3$ | Cl | 156—157 (2.5) | 1.2969 | 1.5223 | 71.64 | 70.51 | 10.48 | 10.18 | 11.17 | 11.66 |
| (VIII) | 1-Phenyl-2-benzoylethenyl diethyl ester of phosphoric acid | $C_2H_5$ | $C_6H_5$ | $C_6H_5$ | H | 208 (3) | — | 1.5490 | — | — | 8.88 | 8.61 | — | — |

two months of storage at room temperature acquired a dark brown color and the odor of acetylacetone. On distillation of this material there was indeed isolated some 10% by weight of acetylacetone; the remainder was the unchanged product. Analogous unsaturated phosphate esters, containing ethyl and n-butyl radicals, were unchanged after storage for several months. In running the reactions of chlorobenzoylacetone with trimethyl and triethyl phosphite there were obtained in 70-80% yields: 1-phenyl-1-buten-3-onyl dimethyl (V) and 1-phenyl-1-buten-3-onyl diethyl (VI) esters of phosphoric acid.

The presence of the double bonds in these esters was proved by bromination. From the low-boiling fractions, obtained during the isolation of (V) and (VI), there separated after a short interval of standing a small quantity of crystals which turned out to be benzoylacetone (m.p. 60-61°; mixed melting point 60°). The amount of benzoylacetone increased with a slow distillation or with higher temperature. Compounds (V) and (VI) acquire a brown color after only a few days storage; during their distillation there distills a considerable amount of benzoylacetone. One may suppose that the facile decomposition of (V) and (VI) is connected with their hydrolysis by the action of atmospheric moisture. Actually a brief heating of compounds (V) and (VI) with water leads to a total hydrolysis and quantitative formation of benzoylacetone. However, special measures taken for the protection of (V) and (VI) from moisture during the process of distillation and storage failed to decrease the rate of their decomposition. Heating (V) and (VI) in sealed ampoules at 150-160° for six hours leads to their almost total decomposition. Benzoylacetone is distilled in considerable amounts from the resulting dark, viscous mass. The process of thermal decomposition of (V) was followed by determination of the change of viscosity of the reaction mixture during the process of heating. Relative viscosity of (V) increases two-fold in five hours and seven-fold in twenty hours during heating of the substance in a thermostat at 155-160° in a sealed viscosimeter (both bulbs of the viscosimeter are connected by means of a sealed-in glass air tube. Measurements of viscosity were made in a thermostat at 20°. Crystallization of benzoylacetone begins during further heating and the reaction mixture, in being cooled, is transformed to a hard crystalline product saturated with a dark tar. A thermographic study of the reaction of benzoylchloroacetone with trimethyl phosphite was carried out (Fig. 1) and a thermogram of decomposition of (V) was run separately (Fig. 2).

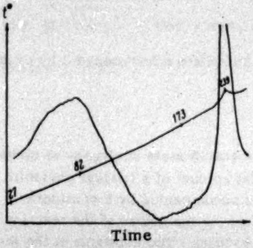


Fig. 1. Thermogram of reaction of benzoylchloroacetone with trimethyl phosphite

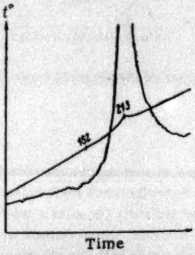
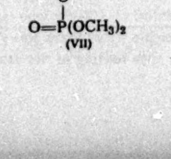


Fig. 2. Thermogram of the decomposition of 1-phenyl-1-buten-3-onyl dimethyl ester of phosphoric acid (V).

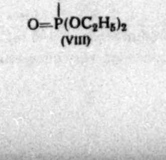
On the first thermogram (Fig. 1) there were recorded two exothermic effects: the first of these corresponds to the reaction of trimethyl phosphite with benzoylchloroacetone, while the second effect, a considerably greater one, corresponds to the thermal decomposition of (V). The latter effect was recorded also in the second thermogram (Fig. 2).

From the reaction of trimethyl phosphite with dichlorobenzoylacetone there was obtained a 72% yield of (VII).



$$\begin{array}{c} C_6H_5-\underset{|}{C}=CClCOCH_3 \\ O \\ | \\ O=P(OCH_3)_2 \end{array}$$

(VII)



$$\begin{array}{c} C_6H_5-\underset{|}{C}=CHCOC_6H_5 \\ O \\ | \\ O=P(OC_2H_5)_2 \end{array}$$

(VIII)

After heating (VII) in a sealed ampoule for four hours at 160°, with a subsequent distillation, there was isolated some chlorobenzoylacetone, with b.p. 146° (14 mm).

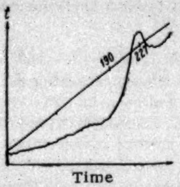
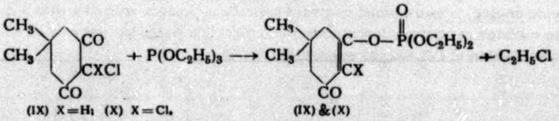


Fig. 3. Thermogram of decomposition of 1-phenyl-2-chloro-1-buten-3-onyl dimethyl ester of phosphoric acid (VII).

On Fig. 3 there is shown the thermogram of decomposition of (VII). The exothermic effect in this case is smaller than in decomposition of (V). As the result of the reaction of triethyl phosphite with dibenzoylchloromethane there was obtained a 20% yield of 1-phenyl-2-benzoylethenyl diethyl ester of phosphoric acid (VIII) in the form of a very viscous liquid. A considerable amount of dibenzoylmethane was also isolated.

In conclusion we reacted triethyl phosphite with chloro- and dichlorodimedones. Considerable decomposition of the reaction products was observed during their distillation. Some dimedone was isolated from the reaction with chlorodimedone and there was obtained, in poor yield and in insufficiently pure state, the 5,5-dimethyl-1-cyclohexen-3-onyl diethyl ester of phosphoric acid (IX). A small amount of crystals of dimedone precipitated from it after a brief interval of standing. Analogous results were obtained with dichlorodimedone. During the distillation of the reaction products there was isolated a considerable amount of chlorodimedone and a small amount of 2-chloro-5,5-dimethyl-1-cyclohexen-3-onyl diethyl ester of phosphoric acid (X). The presence of a double bond in (IX) and (X) was confirmed by bromination.



The mechanism of the thermal decomposition of the unsaturated phosphate esters prepared by us remains unclarified.

## EXPERIMENTAL

The technique of running the reactions (Syntheses of I-VIII). To 0.1-0.15 mole of chloro- or dichloroacetylacetone or benzoylacetone there was added gradually an equimolar amount of a trialkyl phosphite. The reactions began immediately (or after a brief induction period) and were accompanied by a considerable thermal effect. The alkyl chloride, which formed in the reaction, was distilled during the course of the reaction. After heating an hour on a water bath the reaction mixtures were distilled in vacuum. The constants of the products prepared by us and the analytical results are shown in the table.

Thermal decomposition of 1-phenyl-1-buten-3-onyl dimethyl ester of phosphoric acid. 8.5 g of the ester was heated in a sealed ampoule for two hours at 150-160°. The liquid became dark and very viscous. As the result of distillation in vacuum there was isolated 4 g of benzoylacetone, which crystallized in the receiver, and a small amount of an uncrystallizable liquid fraction. The undistillable tarry residue in the flask weighed 3.9 g.

Reaction of triethyl phosphite with 2-chloro-5,5-dimethyl-1,3-cyclohexanedione (chlorodimedone). The reaction was run with 6 g of chlorodimedone and 5.6 g of triethyl phosphite in benzene solution. After heating for two hours on a boiling water bath, the reaction mixture was vacuum distilled. There was obtained 2.1 g of a fraction with b. p. 166-168° (10 mm), $n_D^{20}$ 1.4781. Crystals of dimedone (m. p. 146-147°; mixed m. p. 146°) began to precipitate from this fraction as well as from low-boiling fractions.

Found %: P 10.16. $C_{12}H_{21}O_5P$. Calculated %: P 11.23.

Reaction of triethyl phosphite with 2,2-dichloro-5,5-dimethyl-1,3-cyclohexanedione (dichlorodimedone). To the solution of 13 g of dichlorodimedone in 100 ml of absolute ether there was gradually added 9.4 g of triethyl phosphite. The reaction proceeded very energetically, with boiling of the ether. After 4 hours of heating, the ether was distilled and the residue was distilled in vacuum. After the first distillation there was obtained 10 g of a fraction with b. p. 140-155° (2.5 mm), part of which (3.5 g) crystallized on standing. The crystals turned out to be chlorodimedone (m.p. 157-158°), and no depression was observed in a mixed melting point test. After two distillations of the liquid portion there was obtained 1.3 g of 2-chloro-5,5-dimethyl-1-cyclohexene-3-onyl diethyl ester of phosphoric acid in the form of a very viscous liquid with b.p. 160-161° (2.5 mm); $n_D^{20}$ 1.4818.

Found %: P 10.25, 10.06; Cl 11.13. $C_{12}H_{20}O_5ClP$. Calculated %: P 9.98; Cl 11.43.

The authors express their deep gratitude to A. V. Fuzhenkova for making the thermographic study.

## SUMMARY

1. The reaction of esters of phosphorous acid with chloro- and dichloroacetylacetone, benzoylacetone, dibenzoylmethane and 5,5-dimethyl-1,3-cyclohexanedione (dimedone) were studied.

2. It was shown that all these reactions proceed anomalously forming the corresponding unsaturated esters of phosphoric acid, instead of following the scheme of the Arbuzov rearrangement.

3. Some of the unsaturated esters of phosphoric acid, especially those containing phenyl of cyclohexenyl residues in the composition of the unsaturated radical, suffer a cleavage on being heated and thereby form a β-dicarbonyl compound.

## LITERATURE CITED

[1] B. A. Arbuzov and N. P. Bogonostseva, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1954, 837. *

[2] N. Kreutzkamp and H. Kuser, Naturw. 42, 415, (1955).

[3] A. N. Pudovik and N. M. Lebedeva, Doklady Akad. Nauk SSSR 101, 889 (1955);* A. N. Pudovik, J. Gen. Chem 26, 1426, 1431, 2172 (1956).*

[4] A. N. Pudovik, J. Gen. Chem. 26, 2238 (1956).*

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Kazan State University.

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* Original Russian pagination. See C.B. translation.

# THE PROBLEM OF THE BROMINATION OF CYCLIC KETONES WITH DIOXANE DIBROMIDE

I. V. Machinskaia and A. S. Podberezina

With the objective of preparing α-bromocyclohexanone, we used the method of bromination of cyclohexanone recently developed by L. A. Ianovskaia [1]. Bromination of cyclohexanone is reported [2] to give a monobromocyclohexanone in a yield of 60%.

We brominated cyclohexanone by gradual addition of the ketone to a solution of dioxane dibromide in a mixture of dioxane and absolute ether. An attempt to effect the reaction with equimolar quantities of ketone and dioxane dibromide was unsuccessful – the reaction product broke down when an attempt was made to distil it in vacuo. We observed that the orange solution of dioxane dibromide lost its color when slightly less than 0.5 mole of ketone was added to 1 mole of dioxane dibromide. In later experiments we therefore took the dioxane dibromide and ketone inthe molar ratio of 1 : 0.45. We isolated dibromocyclohexanone from the reaction mixture.

Wallach [3] previously prepared dibromocyclohexanone by the action of bromine on cyclohexanone in glacial acetic acid. He assigned to it the structure of 2,6-dibromocyclohexanone-1. The melting point of our product coincides with that of Wallach's dibromoketone.

Dibromocyclohexanone can be distilled at 4-6 mm without appreciable decomposition. We observed partial decomposition on attempting to distil it at about 40 mm, with formation of more volatile fractions which decolorized bromine water. These products of decomposition of the dibromo compound may have been assumed by L. A. Ianovskaia (who distilled the reaction product at 32 mm) to be monobromocyclohexanone.

We did not succeed in isolating monobromocyclohexanone from the reaction products. If it is formed in the above reaction, its quantity is so small that it distils completely with the first fraction which we did not investigate because the quantity was too small. We obtained the same result on reversing the order of mixing, i.e., on gradually adding a solution of dioxane dibromide to the ketone solution.

During bromination of cyclopentanone with dioxane dibromide we also observed preferential formation of a dibromide of cyclopentanone which had not previously been described.

In this case, however, we also isolated monobromocyclopentanone from the reaction mixture.

Due to the poor stability of monobromocyclopentanone, its elementary composition could not be determined. Reaction with potassium acetate in a medium of glacial acetic acid converted the monobromo compound to α-acetoxycyclopentanone whose properties were identical with those reported in the literature [4].

## EXPERIMENTAL

Bromination of cyclohexanone with dioxane dibromide. 48.6 g of bromine was gradually stirred into 27 g of dioxane. Crystalline, orange dioxane dibromide was formed on cooling. To the latter was added 30 ml of dioxane and 150 ml of absolute ether followed by cyclohexanone in small portions until the reaction mixture had decolorized. This operation was accompanied by heat liberation and the precipitate of dioxane dibromide gradually dissolved. Decolorization of the solution occurred after 13.2 g of cyclohexanone had been added.

The reaction mixture was cooled to room temperature and poured in a fine stream onto ice. The reaction product was extracted with ether. The ether solution was washed with 5% sodium bicarbonate solution and then with water and dried for 1 hour with calcium chloride. The solvent was driven off and the residue distilled in vacuo to give dibromocyclohexanone with b. p. 114-116° (4 mm).[*] Yield 17.3 to 23.7 g (50-69%). The product crystallized after standing for a long time. After recrystallization from alcohol, it had m.p. 106-107°.

Found %: C 28.31, 28.42; H 3.48, 3.42; Br 61.75, 61.68. $C_6H_8OBr_2$. Calculated %: C 28.15; H 3.15; Br 62.44.

The experiment must be completed on the same day; otherwise the product may decompose when distilled in vacuo.

Bromination of cyclopentanone with dioxane dibromide. Mono- and dibromocyclopentanones formed on bromination of cyclopentanone with dioxane dibromide could not both be isolated from the product of a single experiment since the dibromo compound breaks down when the monobromocyclopentanone is distilled. Mono- and dibromocyclopentanones were therefore isolated in different experiments.

Monobromocyclopentanone. 80 g bromine was gradually stirred into 44 g dioxane. A mixture of 44 ml of dioxane and 150 ml of absolute ether was then run in with cooling, followed by 21 g of cyclopentanone in small portions.[**] The mixture was cooled to room temperature and then worked up as in the preceding experiment. Fractional distillation of the reaction product 6 mm gave two main fractions: b.p. 64-70° (14.8 g) and b.p. 70-86° (8 g).[***] When the first fraction was redistilled, it came off nearly completely at 79-83° (15 mm), in agreement with the literature data for monobromocyclopentanone [5]. The yield of the latter was 36%; b.p. 64-70° (6 mm). It is extremely unstable: on standing overnight it nearly completely resinifies.

α-Acetoxycyclopentanone. α-Bromocyclopentanone[****] (7.7 g) (b.p. 79-83° at 15 mm), 9 g of anhydrous potassium acetate and 20 g of glacial acetic acid were heated together on an oil bath at the boil for 2 hours. Water was added to the reaction mixture with cooling, followed by 26.5 g of sodium carbonate. The organic part was extracted with ether; the ethereal solution was washed with 10% sodium carbonate solution (until neutral) and dried with sodium sulfate. After the ether had been driven off, the residue distilled off nearly completely in vacuo (19 mm) at 98-102°, in agreement with data for α-acetoxycyclopentanone [4]. The Beilstein test gave a negative result.

Dibromocyclopentanone. The amounts of starting substances and the procedure were the same as for the preparation of monobromocyclopentanone. After it had been washed with sodium bicarbonate and dried, the ethereal solution of the bromination product was left in a crystallizer overnight. Much hydrogen bromide came off. The residue was a mixture of colorless crystals and a dark, viscous liquid. Alcohol was added to the mixture; the crystals were filtered and washed with alcohol; the colored impurities went completely into solution. After recrystallization from alcohol the m.p. was 68-69° and did not change after another recrystallization.

Found %: Br 65.88. $C_5H_6OBr_2$. Calculated %: Br 66.07.

Weight of dibromocyclopentanone 26.7 g (44.2%).

The reaction mixture resinified when we tried to convert the dibromo compound into the corresponding diacetoxy compound by heating with potassium acetate in a medium of glacial acetic acid. The same result followed attempts to prepare the product of addition of the dibromo compound with pyridine.

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[*] Distillation in a nitrogen stream gave the same result.

[**] After the first portion of cyclopentanone had been added, it was necessary to stir the mixture for a long period before reaction set in; otherwise the addition of a fresh portion of ketone might have led to excessively violent reaction.

[***] The second fraction is evidently a mixture of products of decomposition of the dibromo compound. Special experiments with the crystalline dibromo compound showed that distillation at 6 mm results in breakdown to liquids whose boiling point is slightly higher than that of monobromocyclopentanone.

[****] The bromocyclopentanone had to be reacted immediately after preparation in order to avoid resinification.

## SUMMARY

1. Bromination of cyclohexanone with dioxane dibromide in a mixture of dioxane and absolute ether gives dibromocyclohexanone in 59-69% yield.

2. Bromination of cyclopentanone with dioxane dibromide under the same conditions also leads to the dibromo derivative as the main product; yield 44%; this compound is not described in the literature. At the same time monobromocyclopentanone is formed in a yield of about 36%. The monobromo compound is converted to $\alpha$-acetoxycyclopentanone on heating with potassium acetate in a medium of glacial acetic acid.

## LITERATURE CITED

[1] L. A. Ianovskaia, Proc. Acad. Sci. USSR, 71, 693 (1950);* L. A. Ianovskaia, A. P. Terent'ev and L. I. Belen'kii, J. Gen. Chem. 22, 1594 (1952).*

[2] L. A. Ianovskaia and A. P. Terent'ev, J. Gen. Chem. 22, 1598 (1952).*

[3] O. Wallach, Lieb. Ann. 414, 410 (1917); 437, 173 (1924).

[4] H. Staudinger and L. Ruzicka, Helv. Chim. Acta, 7, 380 (1924).

[5] Kotz, Blendermann, Karpati, and Rosenbuch, Lieb. Ann 400, 51 (1913).

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*Original Russian pagination. See C.B. Translation.

# 5-CHLOROFURYLNITROOLEFINS

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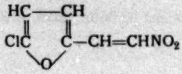
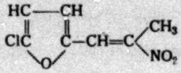
It was previously shown [1, 2] that halofurfurals containing bromine and iodine in the 5 position of the furan ring readily condense with nitroparaffins. In continuation of this work we now report on the products of condensation of 5-chlorofurfural with nitroparaffins. The literature contains quite a large number of syntheses on the basis of 5-chlorofurfural [3], but its condensation with nitroparaffins has not been studied. In recent years years papers and patents have been published on the application of nitroolefins of the aromatic and furan series as insectofungicides [4]. Introduction of a halogen atom into the furan ring stabilizes the latter and enhances the bactericidal activity of the resulting products [1, 5]. For these reasons we should expect the products of condensation of 5-chlorofurfural with nitroparaffins to be of practical interest.

We carried out the condensation of 5-chlorofurfural with nitromethane and nitroethane under various conditions. By a slight modification of the procedure of Moldenhauer [6] we succeeded in preparing 5-chlorofurylnitroethylene (I) in 86% yield. We prepared 5-chlorofurylnitropropene (II) in 79% by the method cited in [1].



(I)



(II)

5-Chlorofurylnitroolefins form light-yellow needles (from alcohol), insoluble in water, soluble in organic solvents, distillable in steam. In the same manner as the halogen in 5-bromo- and 5-iodo derivatives of furan, the chlorine in 5-chlorofurylnitroethylene and 5-chlorofurylnitropropene can be determined by the previously described procedure [2]. It has not yet been possible, however, to replace the chlorine by iodine or the nitro group as is possible with the bromine in 5-bromofurylnitroethylene [1, 2].

The 5-chlorofurylnitroolefins that we prepared exercise an irritant action on the mucous membrane of the nose.

## EXPERIMENTAL

5-Chlorofurylnitroethylene. To a solution (cooled to -12°) of 3.2 g of sodium hydroxide in 16 ml of water and 4 ml of methanol was slowly added (dropwise) 2.81 g of nitromethane. The precipitated sodium salt of nitromethane was put for 10 minutes in a mixture of ice and salt and then completely dissolved by addition of 50 ml of ice water. The solution of the sodium salt of nitromethane was cooled to – 10° and dropwise addition was made, with vigorous stirring, of 5.22 g of 5-chlorofurfural [7] in 12 ml of methanol. After 10-minutes' stirring, the cold (– 10°), transparent solution of the sodium salt of chlorofurylnitroethanol was slowly run with frequent shaking into a cooled (– 5°) solution of 5 ml of concentrated sulfuric acid in 40 ml of water. The lemon-yellow precipitate of 5-chlorofurylnitroethylene was collected after standing for 20 minutes in the cold, thoroughly washed with cold water, and dried in a desiccator over sulfuric acid. Yield 5.98 g (86%), m.p. 103-104°; recrystallization from alcohol gave yellow plates with m.p. 105-106°.

Found %: Cl 20.35. $C_6H_4O_3NCl$. Calculated %: Cl 20.43.

Chlorofurylnitropropene. To a solution (cooled to −10°) of 1.305 g of 5-chlorofurfural and 1 g of nitroethane in 7.5 ml of methanol was added (dropwise with vigorous stirring) 0.6 g of sodium hydroxide in 4 ml of water. A small precipitate appeared after stirring 20 minutes and was completely dissolved by addition of 5 ml of ice water. The cold solution of the sodium salt of 5-chlorofurylnitropropanol was added dropwise with intensive shaking to 3.7 ml of 10% hydrochloric acid cooled to −7°. After 20-minutes' stirring of the mixture (cooled with ice and salt), light-yellow 5-chlorofurylnitropropene was deposited. The filtered product was dried in a desiccator over sulfuric acid and had m.p. 70-72°. Yield 1.485 g (79%). Recrystallization from alcohol gave light-yellow needles with m.p. 74-75°.

Found %: Cl 19.02. $C_7H_6O_3NCl$. Calculated %: Cl 18.90.

## SUMMARY

Condensation of 5-chlorofurfural with nitromethane and nitroethane gave the previously undescribed 5-chlorofurylnitroethylene and 5-chlorofurylnitropropene in yields of 86 and 79% respectively.

## LITERATURE CITED

[1] Z. N. Nazarova, J. Gen. Chem. 24, 575 (1954).*

[2] Z. N. Nazarova, J. Gen. Chem. 25, 539 (1955).*

[3] A. P. Dunlop and F. N. Pertes, The Furans., N. Y., 102 (1953); Ferech, et al., Ref. Zhur. Khim., No. 19249 (1956).

[4] K. Schumann and R. Kaltofen, Ref. Zhur. Khim., Nos. 40677, 40676, 46472 (1955); Moldenhauer and Irion, Ref. Zhur. Khim., No. 66219 (1956); O. Schales and H. A. Graefe, J. Am. Chem. Soc. 74, 4486 (1952).

[5] X. A. Dominguez, J. Slim, and A. Elizondo, J. Am. Chem. Soc. 75, 4581 (1953).

[6] O. Moldenhauer, W. Irion, D. Mastaglio, R. Pfluger and H. Roser, Lieb. Ann. 503, 57 (1953).

[7] F. T. Pozharskii, Sci. Memoirs Rostov State Univ., No. 10 (1957).

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*Original Russian pagination. See C.B. Translation.

# SYNTHESIS OF THIAZOLIDONE DERIVATIVES OF BIOLOGICAL INTEREST

## IX. SYNTHESIS OF 3-DERIVATIVES OF 2,4-THIAZOLIDINEDIONE HYDRAZONE

E. V. Vladzimirskaia

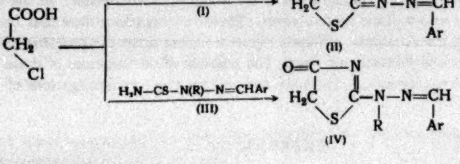
We previously [1] described the synthesis of p-acetaminobenzylidene hydrazones of 2,4-thiazolidinedione and of its 5-derivatives. The molecules of the products contain a hydrogen atom in the 3-position of the thiazolidine ring.

We aimed at synthesizing the 3-derivatives, for which purpose it was necessary to start from 4-derivatives of thibone* R

$$-\overset{4}{N}H-\overset{3}{C}S-\overset{2}{N}H-\overset{1}{N}=CH-C_6H_4-NHCOCH_3$$

and monochloroacetic acid. 4-Derivatives of "thibone" have not been described in the literature, nor have the corresponding products of their condensation with monochloroacetic acid. The introduction of alkyl or aryl substituents into the molecules of therapeutic agents is, however, often accompanied by considerable enhancement of physiological activity.

We prepared 4-methylthiosemicarbazide, 4-allylthiosemicarbazide and 4-phenylthiosemicarbazide by the method of Pulvermacher [2, 3] and condensed them in alcoholic solution with p-acetaminobenzaldehyde to give the corresponding "thibone" derivatives (I, Ar = $CH_3CONHC_6H_4$). The latter substances easily interact with monochloroacetic acid (see equation below) with formation of derivatives of 2,4-thiazolidinedione 2-hydrazone (II).



The 3-derivatives of 2,4-thiazolidinedione p-acetamino-2-benzylidenehydrazone that we synthesized are neutral substances, soluble in alkali solution only with difficulty at the boil.

In order to study the change of properties of preparations on transition from the thiazolidine ring to the thiazoline ring, we prepared benzaldehyde 2-phenylthiosemicarbazone (III, R = Ar = $C_6H_5$) by Pellizzari's method [4] and condensed it with monochloroacetic acid (see equation above). For purposes of comparison we also synthesized and examined the behavior of benzaldehyde thiosemicarbazone, benzaldehyde 4-phenylthiosemicarbazone, 2,4-thiazolidinedione 2-benzaldehydehydrazone, and also 3-phenyl-2,4-thiazolidinedione 2-benzylidenehydrazone (II, R = Ar = $C_6H_5$). The latter substance has not previously been described.

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* p-Acetaminobenzaldehyde thiosemicarbazone.

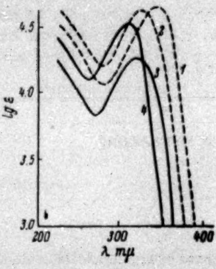

Fig. 1. 1) p-Acetaminobenzaldehyde 4-phenylthiosemicarbazone 2) 3-phenyl-2,4-thiazolidinedione p-acetaminobenzylidene-2-hydrazone, 3) benzaldehyde 4-phenylthiosemicarbazone, 4) $\Delta^2$-4-thiazolinone 2-benzylidenephenylhydrazone.

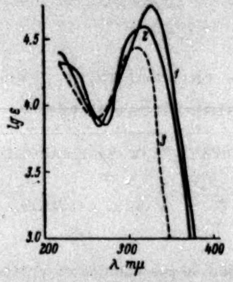

Fig. 2. 1) p-Acetaminobenzaldehyde 4-methylthiosemicarbazone 2) 3-methyl-2,4-thiazolidinedione p-acetaminobenzylidene-2-hydrazone, 3) 2,4-thiazolidinedione 2-benzylidenehydrazone.

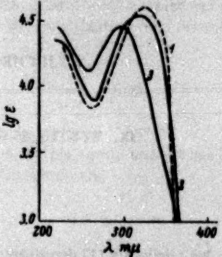

Fig. 3. 1) p-Acetaminobenzaldehyde 4-allylthiosemicarbazone, 2) 3-allyl-2,4-thiazolidinedione p-acetaminobenzylidene-2-hydrazone, 3) benzaldehyde thiosemicarbazone.

The ultraviolet absorption spectra of 4-derivatives of thibone scarcely differ from the corresponding spectra of thibone [5], and only in the case of the phenyl derivative do we observe a slight shift of the characteristic maximum and minimum and also of the long-wave edge of the curve (at $\epsilon$ 1000) in the long-wave direction. The diagram (Figs. 1-3) show that the absorption maxima of these substances are in the 330-337 mμ region and the minima in the 268-275 mμ region. The long-wave edge of the curves for $\epsilon$ 1000 is in the 365-375 mμ region. The absorption spectra of benzaldehyde thiosemicarbazone are very similar to the spectra of thibone and its derivatives but the p-acetamino group displaces the spectra slightly towards the longer waves. The introduction of the phenyl group into the benzaldehyde thiosemicarbazone molecule (Fig. 1) also has no appreciable influence on the change of form of the absorption curves. Since unsubstituted thiosemicarbazide lacks a characteristic maximum [5] in the 310-340 mμ region, the presence of such a maximum in the products of its condensation with aromatic aldehydes is associated with a direct influence of arylidene grouping on the C—S group.

Formation of a thiazolidione or thiazoline ring has no great influence on the absorption spectra in the ultraviolet both in respect of the principal maxima and of the intensity of absorption. At the same time we observe a slight shift of the maxima towards the shorter waves. These investigations show that contrary to our earlier suggestions [5] the study of the ultraviolet absorption spectra cannot solve the problem of the existence of tautomerism in the thiazolidone and thiazolinone rings. The problem of the structure of these rings will have to be solved by chemical and physicochemical methods, and perhaps also by investigations of absorption spectra at other wavelengths.

## EXPERIMENTAL

Synthesis of 4-derivatives of p-acetaminobenzaldehyde thiosemicarbazone. 0.1 mole of 4-phenyl thiosemicarbazide was dissolved in alcohol at the boil and poured into a boiling alcoholic solution of 0.1 mole of p-acetaminobenzaldehyde. The mixture was refluxed for 2 hours. The reaction product, isolated from the reaction mixture after cooling, was filtered and recrystallized from alcohol. The prepared compounds are listed in Table 1.

Synthesis of derivatives of 2,4-thiazolidinedione 2-hydrazone. 5 mmol of the 4-derivative of p-acetaminobenzaldehyde thiosemicarbazone, 5 mmol of monochloroacetic acid and 0.8 g of anhydrous sodium acetate were dissolved in 20-35 ml of glacial acetic acid and refluxed for 2 hours. The resulting transparent solution was diluted (after cooling) with an aqueous solution of sodium acetate. The reaction product was filtered and recrystallized from alcohol. The prepared substances are listed in Table 2.

TABLE 1

4-Derivatives of p-Acetaminobenzaldehyde Thiosemicarbazone

| Preparation No. | Structure | Yield (in %) | Melting point | Nitrogen content (%) | |
|---|---|---|---|---|---|
| | | | | found | calc. |
| 1 | (I), R = $CH_3$ | 30 | 237° | 22.29 | 22.38 |
| 2 | (I), R = $C_3H_5$ | 45 | 223—224 | 20.65 | 20.28 |
| 3 | (I), R = $C_6H_5$ | 48 | 211 | 17.76 | 17.94 |

Similarly we synthesized 3-phenyl-2,4-thiazolidinedione 2-benzylidenehydrazone from benzaldehyde 4-phenylthiosemicarbazone, and also $\Delta^2$-4-thiazolinone 2-benzylidenephenylhydrazone from benzaldehyde 2-phenylthiosemicarbazone. 2,4-Thiazolidinedione 2-benzylidenehydrazone (II, R = H, Ar = $C_6H_5$) was prepared by the method of Chabrier and Cattelain [6] by condensation of monochloroacetic acid with benzaldehyde thiosemicarbazone.

TABLE 2

Derivatives of Thiazolidone and Thiazoline

| Preparation No. | Structure | Yield (in %) | Melting point | Analysis (%) | |
|---|---|---|---|---|---|
| | | | | found | calc. |
| 1 | (II), R = $CH_3$, Ar = $CH_3CONHC_6H_4$ | 48 | 228° | C 53.63,<br>H 5.02,<br>N 19.30 | C 53.67,<br>H 4.86,<br>N 19.30 |
| 2 | (II), R = $C_3H_5$, Ar = $CH_3CONHC_6H_4$ | 76 | 187 | C 56.90,<br>H 5.30,<br>N 17.97 | C 56.94,<br>H 5.10,<br>N 17.71 |
| 3 | (II), R = $C_6H_5$, Ar = $CH_3CONHC_6H_4$ | 55 | 270 | N 16.12 | N 15.90 |
| 4 | (IV), R = Ar = $C_6H_5$ | 86 | 188—189 | C 65.99,<br>H 4.49,<br>N 14.36 | C 65.06,<br>H 4.44,<br>N 14.23 |
| 5 | (II), R = Ar = $C_6H_5$ | 98 | 224 | N 13.89 | N 14.23 |

We carried out the spectrophotometric studies with the help of the SF-4 quartz spectrograph. Solutions of 1-2 mg/100 ml of solvent (ethanol) were prepared.

It is our duty to express thanks to N. M. Turkevich for valuable guidance during the present investigation.

## SUMMARY

1. 3-Derivatives of 2,4-thiazolidinedione 2-arylidenehydrazones were prepared for the first time.

2. It was established that the ultraviolet absorption spectra of $2'$-arylidene derivatives of 2,4-thiazolidinedione 2-hydrazone, both substituted and unsubstituted in the 3-position, do not differ appreciably from the spectra of the original thiosemicarbazones.

## LITERATURE CITED

[1] E. V. Vladzimirskaia and N. M. Turkevich, J. Gen. Chem. 25, 2150 (1955).*

[2] Pulvermacher, Ber. 27, 622 (1894).

[3] Pulvermacher and H. Hempel, Ber. 27, 625 (1894).

[4] G. Pellizzari, Gazz. 37, 1, 611 (1907).

[5] N. M. Turkevich and E. V. Vladzimirskaia, J. Gen. Chem. 27, 1438 (1957).*

[6] P. Chabrier and E. Cattelain, Bull. Soc. Chim. (5), 17, 48 (1950).

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# INTERACTION OF β-CHLOROVINYL KETONES WITH β-DICARBONYL COMPOUNDS

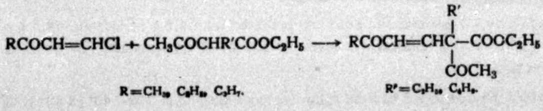
## V. KETOVINYLATION OF α-ALKYL ACETOACETIC ESTERS

N. K. Kochetkov, B. P. Gottikh and L. I. Kudriashov

In preceding communications it was shown that β-chlorovinyl ketones react smoothly with metal derivatives of alkylmalonic [1] and malonic [2] esters with formation of normal products of ketovinylation – γ-ketoalkenyl malonic esters. Since transformations of this new class of substances opened out a route to previously inaccessible types of organic compounds [2, 3], it seemed of interest to broaden the scope of the ketovinylation of compounds with a mobile methylene and methine chain. In the first instance we studied the ketovinylation of α-alkyl acetoacetic esters and now present our results.

Previously we studied the interaction of β-chlorovinyl ketones with acetoacetic ester in presence of potassium carbonate in boiling toluene [4] which showed that the process is complicated by subsequent transformations of the primary products of ketovinylation to give derivatives of alkylsalicylic acids and compounds of unknown structure formed by interaction of two molecules of β-chlorovinyl ketone with one molecule of acetoacetic ester. α-Alkylacetoacetic esters contain only one labile hydrogen atom; such secondary processes are therefore ruled out in the present case, and we should expect formation of only products of normal ketovinylation.

In fact, reaction of β-chlorovinyl ketones with sodium derivatives of α-alkylacetoacetic esters in benzene under conditions similar to those that we described for the ketovinylation of alkylmalonic esters [1] lead smoothly and in good yields to the previously unknown α-alkyl-α-(γ-ketoalkenyl)-acetoacetic esters.



$$RCOCH{=}CHCl + CH_3COCHR'COOC_2H_5 \longrightarrow RCOCH{=}CH\overset{\displaystyle R'}{\underset{\displaystyle COCH_3}{C}}{-}COOC_2H_5$$

$R = CH_3, C_2H_5, C_3H_7$. $R' = C_2H_5, C_4H_9$.

Due to the accessibility of the starting substances and the simplicity of operation, the method that we developed is an extremely convenient one for the preparation of this class of compounds which is of interest and promise for synthetic chemistry.

The prepared compounds are high-boiling oils, stable in storage but easily resinifying on distillation in a too-low vacuum. Their purification must therefore be effected with suitable precautions (see Experimental).

The structures of the prepared compounds are confirmed by analyses. Hydrogenation of one of the compounds – ethyl-(3-ketobutenyl-1)-acetoacetic ester – indicates the presence of one double bond in the products of ketovinylation. An alternative possibility of ketovinylation at the oxygen (by analogy with known cases of acylation of acetoacetic esters with acid chlorides) must be rejected since the products that we prepared are stable towards mineral acids under mild conditions, whereas it is well known that β-substituted vinyl ketones of the type of RCOCH=CH-X, where X = OR, OAr (for example phenoxyvinyl ketones and alkoxyvinyl ketones) are easily hydrolyzed under such conditions, the ketovinyl residue being split off with formation of a symmetrical triacyl benzene (for example [5]). Moreover, the structure of the prepared compounds is confirmed by some of their transformations which we shall report on in later communications.

## EXPERIMENTAL

Ethyl-(3-ketobutenyl-1)-acetoacetic ester. 7.5 g of sodium finely dispersed in xylene and 300 ml of dry benzene were placed in a three-necked flask fitted with stirrer, reflux condenser and dropping funnel; dropwise addition of 54 g of ethyl acetoacetic ester with stirring was then made. The reaction mixture was slowly heated on a water bath; after the whole of the ethyl acetoacetic ester had been added, the mixture was boiled until the whole of the sodium had gone into solution (2-3 hours). It was then cooled with ice water. A solution of 30 g of methyl β-chlorovinyl ketone in 75 ml of dry benzene was then added dropwise (vigorous stirring) in the course of 1-1.5 hours. (A flask of adequate size must be used because considerable foaming occurs during the addition of the ketone.) After the whole of the ketone had been added, the cooling was stopped and the reaction mixture boiled for 2.5-3 hours and then washed with water (2 × 100 ml). The wash waters were extracted with ether and the ether extracts were combined with the benzene solution. The combined ether-benzene extracts were dried with sodium sulfate, the solvents were driven off and the residue distilled in vacuo. The fraction boiling at 130-145° (5 mm) was collected.*

After 3 distillations the compound had the following constants: b.p. 108-110° (1 mm), $d_4^{20}$ 1.0550, $n_D^{20}$ 1.4670, $MR_D$ 59.51; calculated 58.92. Yield 42.0 g (64.5%).

Found %: C 63.91, 63.81; H 8.07, 8.12. $C_{12}H_{18}O_4$. Calculated %: C 63.71; H 8.02.

Ethyl-(3-ketobutenyl-1)-acetoacetic ester is a colorless oil with a characteristic odor, miscible with organic solvents, insoluble in water. It has a long duration of stability.

Ethyl-(3-ketopenten-1-yl-1)-acetoacetic ester is similarly prepared from 7 g of sodium, 52 g of ethylacetoacetic ester and 36 g of ethyl β-chlorovinyl ketone in 330 ml of dry benzene. The fraction with b.p. 128-135° (3 mm) was collected.

After 3 distillations the substance had the following constants: b.p. 115-117° (1 mm), $d_4^{20}$ 1.0415, $n_D^{20}$ 1.4665, $MR_D$ 64.01; calculated 63.44. Yield 43.5 g (52%).

Found %: C 65.32, 65.20; H 7.99, 8.05. $C_{13}H_{20}O_4$. Calculated %: C 64.97; H 8.39

Ethyl-(3-ketohexen-1-yl-1)-acetoacetic ester was prepared from 6 g of sodium, 43 g of ethyl acetoacetic ester and 31 g of propyl β-chlorovinyl ketone in 300 ml of dry benzene. The fraction with b.p. 151-160° (5 mm) was collected.

After 3 distillations the compound had the following constants: b.p. 120-122° (1 mm), $d_4^{20}$ 1.0270, $n_D^{20}$ 1.4657, $MR_D$ 68.53; calculated 68.03. Yield 42 g (72%).

Found %: C 66.02, 65.89; H 8.53, 8.56. $C_{14}H_{22}O_4$. Calculated %: C 66.12; H 8.72.

n-Butyl-(3-ketobutenyl-1)-acetoacetic ester was prepared from 4.8 g of sodium, 44.6 g of n-butylacetoacetic ester and 20.9 g of methyl β-chlorovinyl ketone in 200 ml of dry benzene. The fraction with b.p. 153-164° (6 mm) was collected.

After 3 distillations the compound had the following constants: b.p. 139-140° (2 mm), $d_4^{20}$ 1.0274, $n_D^{20}$ 1.4662, $MR_D$ 68.58; calculated 68.06. Yield 27.9 g (55%).

Found %: C 65.98, 66.13; H 8.77, 8.90. $C_{14}H_{22}O_4$. Calculated %: C 66.12; H 8.72.

n-Butyl-(3-ketohexen-1-yl-1)-acetoacetic ester was prepared from 3 g of sodium, 26 g of n-butylacetoacetic ester and 15 g of propyl β-chlorovinyl ketone in 150 ml of dry benzene. On distillation in vacuo the fraction with b.p. 137-145° (2 mm) was collected.

After 3 distillations in vacuo the compound had: b. p. 137-138° (1 mm), $d_4^{20}$ 1.0007, $n_D^{20}$ 1.4650, $MR_D$ 78.19; calculated 77.30. Yield 24 g (75%).

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* Distillation is best effected from a Claisen flask without a column and with a low side-tube. At first it is necessary to distill the substance rapidly with addition of hydroquinone and preferably in a current of inert gas. This enables the yield to be raised by 10-15%.

Found %: C 68.30, 68.56; H 9.48, 9.40. $C_{16}H_{26}O_4$. Calculated %: C 68.06; H 9.28.

Hydrogenation of ethyl-(3-ketobutenyl-1)-acetoacetic ester. 28.5 g of ethyl-(3-ketobutenyl-1)-acetoacetic ester was hydrogenated in 100 ml of ether over palladium deposited on barium sulfate. After 3045 ml of hydrogen (0°, 760mm) had been absorbed, hydrogenation was stopped (the theoretical requirement was 3070 ml of hydrogen). The catalyst was filtered off, the ether was distilled off, and the residue was distilled in vacuo. The fraction with b.p. 115-117° (3 mm) was collected.

After 3 distillations the substance had: b.p. 104-105° (1 mm), $d_4^{20}$ 1.0429, $n_D^{20}$ 1.4500, $MR_D$ 58.84; calculated 59.29. Yield 28.0 g (quantitative).

Found %: C 63.45; H 8.87. $C_{12}H_{20}O_4$. Calculated %: C 63.13; H 8.83.

Ethyl-(3-ketobutyl)-acetoacetic ester is a colorless oil, miscible with organic solvents, insoluble in water, and stable in storage.

## SUMMARY

The interaction of β-chlorovinyl ketones with α-alkylacetoacetic esters was studied. The products are α-alkyl-α-(γ-ketoalkenyl)-acetoacetic esters. The reaction is a convenient means of synthesis of compounds of this new class (yield 50-75%).

## LITERATURE CITED

[1] N. K. Kochetkov and L. I. Kudriashov, J. Gen. Chem. 26, 851 (1956).*

[2] N. K. Kochetkov and L. I. Kudriashov, J. Gen. Chem. 27, 248 (1957).*

[3] N. K. Kochetkov, L. I. Kudriashov and R. A. Aleeva, J. Gen. Chem. 27, 2166 (1957).*

[4] N. K. Kochetkov, L. I. Kudriashov and A. N. Nesmeianov, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1955, 809.*

[5] N. K. Kochetkov, Prog. Chem. Sci. 24, 32 (1955).

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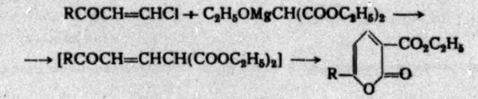
# INTERACTION OF β-CHLOROVINYL KETONES WITH β-DICARBONYL COMPOUNDS

## VI SYNTHESIS OF SOME DERIVATIVES OF α-PYRONES

N. K. Kochetkov and L. I. Kudriashov

In the preceding communications [1, 2] we described the ketovinylation of malonic and alkylmalonic esters. Interaction of ethoxymagnesium malonic ester with β-chlorovinyl ketones led to formation of γ-ketoalkenylmalonic esters, which underwent cyclization under the action of acetyl chloride or certain acidic reagents and formed 6-alkyl-3-carbethoxy-α-pyrones [2]. This new route to α-pyrones has, however, defects associated with certain experimental difficulties during the synthesis and isolation of γ-ketoalkenylmalonic esters, as well as with the conditions of cyclization. The latter leads to severe resinification of the reaction mixture if the γ-ketoalkenylmalonic ester is not previously purified.

We recently developed a new and more convenient variant of the synthesis of α-pyrones which may be described briefly as follows: A toluene solution of the β-chlorovinyl ketone was added to ethoxymagnesium malonic ester prepared in the minimum quantity of alcohol; after the reaction was completed by heating the perfectly homogeneous mixture is decomposed with glacial acetic acid, and the resulting γ-ketoalkenylmalonic ester (without purification) is cyclized to the α-pyrone by heating with acetic anhydride or acetyl chloride (the latter gives slightly better results).


$RCOCH{=}CHCl + C_2H_5OMgCH(COOC_2H_5)_2 \longrightarrow$
$\longrightarrow [RCOCH{=}CHCH(COOC_2H_5)_2] \longrightarrow$
$CO_2C_2H_5$
R
O
O

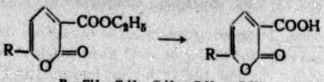
$R = C_3H_7,\ C_5H_{11},\ C_7H_{15},\ C_6H_5.$

A careful investigation of the reaction mixture, carried out during synthesis of the propyl homolog, showed that a very small quantity (0.5-1%) of a substance with m. p. 104-104.5° (not a pyrone) is formed at the same time as the pyrone under the reaction conditions. Analysis and determination of molecular weight of the product of saponification indicated the formula $C_{17}H_{20}O_4$. Its structure was not investigated; however, it evidently contains an aromatic ring since treatment with nitration mixture readily gives a nitro derivative containing an aromatic group. Similar secondary products are evidently also formed during synthesis of other homologs; in all cases, however, they are formed in such small quantity that they do not hinder to the slightest degree the separation of the pyrone, and they do not detract from the proposed value of our method of synthesis.

The new procedure thus makes superfluous the isolation of γ-ketoalkenyl malonic esters in the pure form; this considerably simplifies the whole synthesis which is essentially a direct synthesis of derivatives of α-pyrone (in yields of about 40%) from β-chlorovinyl ketones.

By this method we prepared 6-phenyl-, 6-propyl-, 6-amyl- and 6-heptyl-3-carbethoxy-α-pyrones. The two last substances have not previously been described.

The new method makes 6-alkyl-3-carbethoxy-α-pyrones easily accessible substances; on their basis we were therefore able to prepare several derivatives of that type with the objective of throwing light upon the physiological activity of derivatives of α-pyrone. No information on this question has appeared in the literature, although the high physiological activity of derivatives of corresponding condensed systems – coumarin and chromone* is well-known. With this objective we first studied the possibility of preparing derivatives of 6-alkyl-α-pyrone-3-carboxylic acids. Hydrolysis of the prepared 6-alkyl-3-carbethoxy-α-pyrones is easily effected by heating them with concentrated hydrochloric acid (yield about 70%).



$R = CH_3, C_3H_7, C_5H_{11}, C_7H_{15}, C_6H_5.$

This ease of hydrolysis depends on the nature of the substituent in the 6-position. Thus, hydrolysis of 6-methyl-3-carbethoxy-α-pyrone requires a half-hour's heating with concentrated hydrochloric acid at 60°; the heptyl homolog ($R = C_7H_{15}$) is saponified by one-and-a-half-hour's heating at 70°, while the phenyl homolog ($R = C_6H_5$) already requires boiling for one and a half hours with concentrated hydrochloric acid. It should be noted that 6-alkyl-3-carbethoxy-α-pyrones can also be hydrolyzed with concentrated hydrochloric acid at room temperature, but the operation is then a very lengthy one.

The resulting 6-substituted α-pyronecarboxylic acids are colorless, crystalline substances, differing from one another in their behavior on heating. Thus, 6-methyl-α-pyrone-3-carboxylic acid undergoes decarboxylation on melting or on heating in solution at above 70°; its aliphatic analogs withstand heating in solutions to 100°, while 6-phenyl-α-pyrone-3-carboxylic acid can even be distilled unchanged in vacuo.

An attempt to prepare substituted amides of these acids by the direct action of amines on substituted 3-carbethoxy-α-pyrones was unsuccessful, because the reaction is then directed towards cleavage of the pyrone ring (this behavior will be the subject of a later communication). The preparation of compounds of the type in question, which we carried out in the case of 6-methyl-α-pyrone-3-carboxylic acid, could only be realized via the corresponding acid chloride. The latter was obtained by the action of thionyl chloride on the corresponding acid. Treatment of the acid chloride with aniline and diethylamine gave the anilide and diethylamide of 6-methyl-α-pyrone-3-carboxylic acid. Treatment of the acid chloride with hydrazine gave only N,N'-bis-(6-methyl-α-pyronyl-3)-hydrazine, and a monosubstituted hydrazide could not be isolated. Futher investigation of the acid chlorides of α-pyronecarboxylic acids led to the preparation of a wide range of the corresponding derivatives. All of the prepared compounds were subjected to pharmacological tests, the results of which will be communicated separately.

## EXPERIMENTAL

6-Propyl-3-carbethoxy-α-pyrone. 6 g of magnesium was put into a three-necked flask fitted with stirrer, dropping funnel and reflux condenser (a calcium chloride tube topped the latter); the magnesium was activated by heating with a crystal of iodine. Dropwise addition was then made of a mixture of 35 ml of malonic ester and 10 ml of anhydrous alcohol. After the violent reaction had subsided, another mixture of 10 ml of malonic ester and 25 ml of anhydrous alcohol was added and the mass was boiled until the whole of the magnesium had dissolved (about 2 hours); it was then cooled in an ice bath, and dropwise addition was made (vigorous stirring) in the course of an hour of a solution of 26.5 g of propyl β-chlorovinyl ketone in 20 ml of anhydrous toluene. In some cases a precipitate of ethoxymagnesium malonic ester came down on cooling and the stirring was stopped. In such cases the reaction was started without stirring, but after introduction of only about one-fifth of the total quantity of ketone, the reaction mixture became sufficiently dilute to permit stirring. After the propyl β-chlorovinyl ketone had been added, the reaction mass was stirred for 30 minutes at room temperature and then heated for 1.5 hours on a boiling water bath. After cooling, 40 ml of glacial acetic acid was added, followed by 100 ml of water (the aqueous layer must have a weakly acidic reaction to litmus), and the resulting oil was extracted with toluene (3 x 30 ml). The toluene was distilled off; the thermometer in the liquid registered 140° at the end of the distillation. 100 ml of acetyl chloride was added to the residue and the mixture was boiled for 4 hours. After cooling, the acetyl chloride was added to the residue and the mixture was boiled for 4 hours. After cooling, the acetyl chloride was distilled off; the residue was then distilled, the 154-192° (3-5 mm) fraction being collected (28.0 g). Distillation with glass wool is recommended in view of the considerable decomposition during the operation. Redistillation gave 18.1 g (43%) of 6-propyl-3-carbethoxy-α-pyrone.

B.p. 145-148° (1 mm), $d_4^{20}$ 1.1285, $n_D^{20}$ 1.5170 (the erroneous value of 1.5770 was previously reported [1]).

Found %: C 62.88, 62.95. H 6.79, 6.84. $C_{11}H_{14}O_4$. Calculated %: C 62.84; H 6.71.

A white crystalline substance with m. p. 104-104.5° (from alcohol) came down after 3-5 days from the higher fractions after separation of the 6-propyl-3-carbethoxy-α-pyrone.

Found %: C 71.17, 71.05; H 7.22, 7.29. $C_{17}H_{20}O_4$. Calculated %: C 70.81; H 6.99.

**6-Amyl-3-carbethoxy-α-pyrone.** Prepared under the same conditions (see preceding experiment) from 6 g of magnesium, 45 ml of malonic ester and 32.1 g of amyl β-chlorovinyl ketone, with 35 ml of anhydrous alcohol and 100 ml of acetyl chloride. The 159-194° (2-4 mm) fraction (33.1 g) was collected on distillation. A redistillation gave 21.3 g (44%) of 6-amyl-3-carbethoxy-α-pyrone.

B.p. 147-150° (0.5 mm), 165-166° (1 mm), $d_4^{20}$ 1 0994, $n_D^{20}$ 1.5128.

Found %: C 65.49, 65.58; H 7.67, 7.60. $C_{13}H_{18}O_4$. Calculated %: C 65.53; H 7.62.

**6-Heptyl-3-carbethoxy-α-pyrone.** Similarly prepared from 3 g of magnesium, 23 ml of malonic ester and 18.85 g of heptyl β-chlorovinyl ketone, using 17 ml of alcohol and 50 ml of acetyl chloride. The fraction with b.p. 173-198° (2-4 mm) was collected on distillation (16.4 g). Redistillation gave 10.2 g (38.3%) of 6-heptyl-3-carbethoxy-α-pyrone.

B.p. 159-162° (0.5 mm). After redistillation b.p. 161-162° (0.5 mm), $d_4^{20}$ 1.0555, $n_D^{20}$ 1.5079.

Found %: C 67.83, 67.71; H 8.69, 8.48. $C_{15}H_{22}O_4$. Calculated %: C 67.64; H 8.33.

**6-Phenyl-3-carbethoxy-α-pyrone.** Similarly prepared from 1.9 g of magnesium, 16 ml of malonic ester and 9.7 g of phenyl β-chlorovinyl ketone, with use of 8 ml of alcohol and 25 ml of acetyl chloride. After the acetyl chloride had been removed from the reaction mixture, the fraction coming off up to 110° (6 mm) was taken off in vacuo; the residue was dissolved in a little methanol, and 6-phenyl-3-carbethoxy-α-pyrone was brought down with water. Yield 7.7 g (55%), m.p. 105° (from methanol) [3].

**6-Alkyl-α-pyrone-3-carboxylic acids.** 0.91 mole of 6-alkyl-3-carbethoxy-α-pyrone was heated with 5.5 ml of concentrated hydrochloric acid (50 ml in the case of the phenyl homolog); after cooling, the mass was diluted with 4 times the quantity of water, dried in vacuo over phosphorus pentoxide and recrystallized. Reaction conditions and properties of the pyronecarboxylic acids are presented in the table.

6-Alkyl-α-pyrone-3-carboxylic Acids

| R | Period of heating and temperature | Yield (in %) | Melting point | Solvent for recrystallization | Found (%) |  | Calculated (%) |  |
|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  | C | H | C | H |
| $CH_3$ | 30 min. 60—64° | 70.0 | 163—164° (разл.) | Dioxane, 80° | 54.71,<br>54.84 | 4.05,<br>3.99 | 54.55 | 3.92 |
| $C_3H_7$ | 30 min. 70 | 74.6 | 113 | Alcohol | 59.38,<br>59.54, | 5.48,<br>5.51 | 59.34 | 5.53 |
| $C_5H_{11}$ | 75 min. 70 | 76.2 | 120—121 | Alcohol | 62.86<br>62.76 | 6.70,<br>6.72 | 62.84 | 6.71 |
| $C_7H_{15}$ | 120 min. 70 | 58.2 | 119—120 | Alcohol | 65.55,<br>65.66 | 7.76,<br>7.78 | 65.53 | 7.62 |
| $C_6H_5$ | 90 min., boiling | 77.0 | 170—171°* | Glacial acetic acid | 66.81,<br>66.62. | 3.88,<br>3.84 | 66.67 | 3.73 |

**Anilide of 6-methyl-α-pyrone-3-carboxylic acid.** 0.4 g of 6-methyl-α-pyrone-3-carboxylic acid and 6 ml of freshly distilled thionyl chloride were heated for 1 hour at 40°; the next day the product was evaporated in vacuo, the residue was dissolved in 10 ml of absolute ether, and 0.5 g of aniline in 5 ml of absolute ether was added dropwise to the solution. After 30 minutes the aniline hydrochloride was filtered off, the ethereal solution was evaporated, and the anilide of 6-methyl-α-pyronecarboxylic acid was obtained. Yield 0.32 g (53%). m. p. 146° (from aqueous alcohol).

Found %: N 5.97, 6.38. $C_{13}H_{11}O_3N$. Calculated %: N 6.11.

6-Methyl-α-pyrone-3-carboxylic acid chloride. 4.8 g of 6-methyl-α-pyrone-3-carboxylic acid and 7 ml of freshly distilled thionyl chloride were heated for 6 hours at 40-50°; the solid, crystalline mass was recrystallized from 13 ml of anhydrous benzene, washed with 2 ml of anhydrous benzene, and dried in vacuo over paraffin wax. Yield of 6-methyl-α-pyrone-3-carboxylic acid chloride 4.6 g (86.8%), m.p. 127-127.5° (from benzene).

Found %: Cl 20.28, 20.35. $C_7H_5O_3Cl$. Calculated %: Cl 20.55.

6-Methyl-α-pyrone-3-carboxylic acid diethylamide. A solution of 4.2 ml of diethylamine in 20 ml of absolute benzene was added with cooling to a solution of 3.5 g of 6-methyl-α-pyrone-3-carboxylic acid chloride in 60 ml of absolute ether. After 3 hours, the diethylamine hydrochloride was filtered off, the filtrate was evaporated, and the diethylamide of 6-methyl-α-pyronecarboxylic acid was isolated in a yield of 3.2 g (76.2%), m.p. 57-58° (from a mixture of benzene and ligroine).

Found %: C 62.85, 62.80; H 7.19, 7.17. $C_{11}H_{15}O_3N$. Calculated %: C 63.14; H 7.23.

N,N'-Bis-(6-methyl-α-pyronyl-3)-hydrazine. 2.2 ml of hydrazine hydrate was added dropwise with cooling and vigorous stirring to a solution of 3.5 g of 6-methyl-α-pyrone-3-carboxylic acid chloride in 80 ml of absolute benzene. After two hours the reaction mass was heated to the boil; after cooling, the precipitate of N,N'-bis-(6-methyl-α-pyronyl-3)-hydrazine was filtered off and washed twice with hot benzene in water. Yield 2.3 g (38%). After recrystallization from glacial acetic acid, a specimen did not melt on heating to 400°.

Found %: C 55.04, 55.14; H 3.98, 4.07. $C_{14}H_{12}O_6N_2$. Calculated %: C 55.26; H 3.98.

## SUMMARY

1. A direct method was developed for the synthesis of 6-substituted 3-carbethoxy-α-pyrones by condensing β-chlorovinyl ketones with ethoxymagnesium malonic ester followed by cyclization of the reaction product by treatment with acetyl chloride (yield 40%).

2. The prepared 6-alkyl(aryl)-3-carbethoxy-α-pyrones were hydrolyzed to the corresponding acids by treatment with concentrated hydrochloric acid.

3. Some derivatives of 6-methyl-α-pyrone-3-carboxylic acid were prepared.

## LITERATURE CITED

[1] N. K. Kochetkov and L. I. Kudriashov, J. Gen. Chem. 27, 248 (1957).•

[2] N. K Kochetkov and L. I. Kudriashov, J. Gen. Chem. 26, 851 (1956).•

[3] J. Walker, J. Chem. Soc. 1939, 120.

[4] R. Kallf, Rec. trav. chim. 46, 594 (1927).

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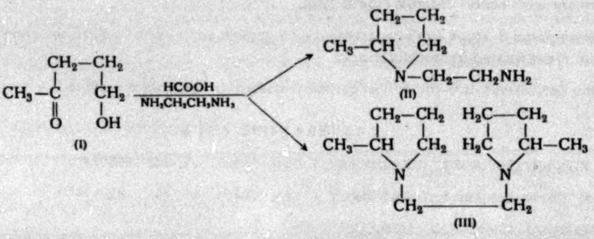
# SYNTHESIS AND PROPERTIES OF PYRROLIDINE BASES

## IV. 2-METHYL-N-β-AMINOETHYLPYRROLIDINE AND SOME OF ITS TRANSFORMATIONS

A. P. Terent'ev, M. A. Volodina and V. G. Mishina

In the preceding communications[1-3] we showed that γ-ketoalcohols are an accessible starting point for the preparation of pyrrolidine and pyrrolidone bases. Some of the compounds that we prepared in these series exhibited considerable physiological activity (tests were carried out in the Institute of Pharmacology of the Academy of Medical Sciences of the USSR). This prompted us to undertake the synthesis of 2-methyl-N-β-aminoethylpyrrolidine and to study some of its reactions. The present investigation was of interest from the viewpoint of synthesis of compounds with possible pharmacological activity.

By reaction of γ-acetopropyl alcohol (I) with N,N'-ethyleneformamide we obtained a 60% yield of 2-methyl-N-β-aminoethylpyrrolidine (II) together with 2,2-dimethyl-N,N'-dipyrrolidineethane (III). Preliminary tests of 2-methyl-N-β-aminoethylpyrrolidine indicated considerable physiological activity.

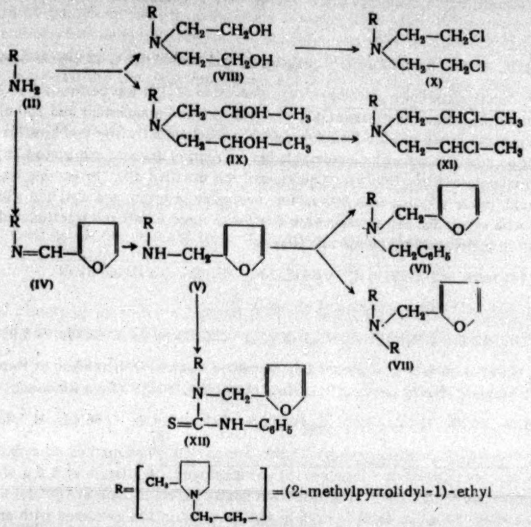


We studied some transformations of 2-methyl-N-β-aminoethylpyrrolidine (II). Its reaction with furfural gave 2-methyl-N-β-furylideneaminoethylpyrrolidine (IV), reduction of which by magnesium in methanol (Zechmeister's method [4]) gave 2-methyl-N-β-furylaminoethylpyrrolidine (V). We obtained the corresponding tertiary amines by reacting (V) with benzyl chloride and 2-methyl-β-chloroethylpyrrolidine: N-2-furyl-N-benzyl-β-(2-methylpyrrolidyl-1)-ethylamine (VI) and N-2-furyl-N-(2-methylpyrrolidyl-1-ethyl)-β-(2-methylpyrrolidyl-1)-ethylamine (VII).

Treatment of (V) with phenyl isocyanate gave N-phenyl-N'-2-(2-methyl-N-pyrrolidyl)-ethyl-N'-furylthiourea (XII).

Reaction of ethylene oxide and propylene oxide with (II) gave the amino alcohols N,N-β,β'-dihydroxydiethyl-β-(2-methylpyrrolidyl-1)-ethylamine (VIII) and N,N-β,β'-dihydroxydipropyl-β-(2-methylpyrrolidyl-1)-ethylamine (IX), which were subsequently converted to the corresponding β-chloroalkylamines: N,N-(β,β'-dichlorodiethyl)-β-(2-methylpyrrolidyl-1)-ethylamine (X) and N,N-(β,β'-dichlorodipropyl)-β-(2-methylpyrrolidyl-1)-ethylamine (XI).

All of the above-described transformations can be represented by the following scheme:



## EXPERIMENTAL

We used commercial acetopropyl alcohol which was distilled in vacuo.

B. p. 114-115° (30 mm), $n_D^{20}$ 1.4395, $d_4^{20}$ 1.0068, $MR_D$ 26.69. Literature data [5]: b. p. 115-116° (30 mm), $n_D^{20}$ 1.4390.

2-Methyl-N-β-aminoethylpyrrolidine (II) and 2,2-dimethyldipyrrolidylethane (III). 40.8 g of γ-acetopropyl alcohol was heated with the formyl derivative of ethylenediamine (from 96 g of ethylenediamine) and 4 g of nickel powder for 20-25 hours at 130-180° (the temperature gradually rose with progressive weakening of the stream of evolved carbon dioxide). After cooling, the reaction mixture was hydrolyzed by boiling for 2 hours with 200 ml of concentrated hydrochloric acid and then neutralized with 40% sodium hydroxide solution until it had a strongly alkaline reaction. The reaction product was extracted with ether; the ethereal extracts were dried with fused alkali and fractionated. Yield 30 g (60.4%) of compounds (II).

B.p. 56-58° (8 mm), $n_D^{20}$ 1.4640, $d_4^{20}$ 0.88725, $MR_D$ 39.87; calculated 39.67.

Dipicrate, m.p. 222-224°.

Found %: C 38.77, 38.69; H 3.88, 3.82. $C_{19}H_{22}O_{14}N_8$. Calculated %: C 38.93; H 3.78.

In addition to (II), 8 g (10%) of (III) was isolated.

B.p. 110-115° (8 mm), $n_D^{20}$ 1.4730, $d_4^{20}$ 0.90078, $MR_D$ 61.20; calculated 61.14.

Dipicrate, m.p. 245-247°.

Found %: C 43.66, 43.71; H 4.75, 4.62. $C_{24}H_{30}O_{14}N_8$. Calculated %: C 44.19; H 4.62.

2-Methyl-N-(β-furylideneaminoethyl)-pyrrolidine (IV). Compound (IV) was prepared by the method described by Hansal [6] for N-furylidene-o-anisidine [6]. 12.8 g of compound (II) was mixed with 9.6 g of freshly distilled furfural. The mixture was left for 2 hours at room temperature and then held for 2 hours at 30-35°.

Distillation in vacuo gave 18 g (90%) of 2-methyl-N-β-furylideneaminoethylpyrrolidine.

B.p. 143-144° (4 mm), $n_D^{20}$ 1.5250, $d_4^{20}$ 1.0211, $MR_D$ 62.27; calculated 61.97.

Dipicrate (from acetone), m. p. 245°.

Found %: C 43.25, 43.42; H 3.59, 3.57. $C_{24}H_{24}O_{15}N_8$. Calculated %: C 43.38; H 3.64.

**2-Methyl-N-(β-furylaminoethyl)-pyrrolidine (V)** Reduction of (IV) was performed by Zechmeister's [4] and Hansal's [7] methods, 13 g of compound (IV), 10.5 g of purified magnesium and 150 mg of anhydrous methyl alcohol were put into a two-necked flask fitted with a mechanical stirrer and a reflux condenser. After a short time the reaction commenced with considerable heat evolution and was completed in 15-20 minutes, the magnesium going completely into solution. The alcohol was distilled off; the residue was decomposed with ice and 40% acetic acid, made alkaline with 40% sodium hydroxide solution, and distilled with steam. The distillate was extracted with ether, and the extracts were dried with fused alkali and fractionated to give 4 g (30%) of 2-methyl-N-β-(N'-furylaminoethyl)-pyrrolidine (V).

B. p. 152-154° (15 mm), $n_D^{20}$ 1.4910, $d_4^{20}$ 0.9886, $MR_D$ 61.02; calculated 61.46.

Dipicrate, m.p. 144-145° (from acetone and alcohol).

Found %: C 43.00, 43.15; H 4.33, 4.23. $C_{24}H_{26}O_{15}N_8$. Calculated %: C 43.24; H 3.93.

Heating of 1 g of (V) with 0.65 g of phenyl isothiocyanate resulted in formation of N-phenyl-N'-2-(2-methyl-N-pyrrolidyl)-ethyl-N'-furylthiourea (XII). Yield 86%, m. p. 90-91° (from alcohol).

Found %: C 66.26, 66.41; H 7.41, 7.37. $C_{19}H_{25}ON_3S$. Calculated %: C 66.44; H 7.33.

**N-2-Furyl-N-benzyl-β-(2-methylpyrrolidyl-1)-ethylamine (VI).** The method described in the literature for the preparation of tertiary pyrrolidylethylamines [8] was employed. A mixture of 5.2 g of (V), 5.3 g of anhydrous sodium carbonate and 6.3 g of benzyl chloride was heated on an oil bath at 160° for 6 hours. After the reaction mixture had cooled, 70 ml of water was run in and the solution was extracted with ether. The ethereal extracts were dried over fused caustic alkali. Two distillations gave 5.6 g (40%) of (VI).

B.p. 194-196° (10 mm), $n_D^{20}$ 1.5365, $d_4^{20}$ 1.0334, $MR_D$ 90.11; calculated 90.46.

Dipicrate (from 50% acetic acid), m.p. 165-166°.

Found %: C 49.07, 49.32; H 4.00, 4.32. $C_{31}H_{32}O_{15}N_8$. Calculated %: C 49.20; H 4.10.

**N-2-Furyl-N-(2-methyl-β-ethylpyrrolidyl-1-)-ethylamine (VII).** Preparation was on the same lines as for (VI), starting from 5.2 g of (V), 5.3 g of anhydrous sodium carbonate and 7.4 g of 2-methyl-N-β-chloroethylpyrrolidine. 5.5 g (35%) of (VII) was obtained.

B.p. 182-183° (5 mm), $n_D^{20}$ 1.4970, $d_4^{20}$ 0.9777, $MR_D$ 95.62; calculated 95.87.

Dipicrate (from 50% acetic acid), m.p. 133-135°.

Found %: C 47.73, 47.98; H 4.90, 5.20. $C_{31}H_{39}O_{15}N_9$. Calculated %: C 47.87; H 5.00.

**N,N-β,β'-Dihydroxydiethyl-β-(2-methylpyrrolidyl-1)-ethylamine (VIII).** 12.8 g of (II) was heated in an ampoule with 35.4 g of ethylene oxide in 150 ml of ethyl alcohol at 100° for 6 hours. The alcohol was taken off in vacuo and the residue was fractionated to give 18 g (83%) of (VIII).

B.p. 185-190° (10 mm), $n_D^{20}$ 1.4885, $d_4^{20}$ 1.0218, $MR_D$ 61.05; calculated 61.70.

Dipicrate (from acetone), m.p. 167-168°.

Found %: C 41.77, 41.66; H 4.76, 4.87. $C_{23}H_{30}O_{16}N_8$. Calculated %: C 40.98; H 4.48.

**N,N-(β,β'-dihydroxydipropyl)-β-(2-methylpyrrolidyl-1)-ethylamine (IX)** was similarly prepared from 12.8 g of (II) and 46.4 g of propylene oxide. Yield 21 g (84%) of substance (IX).

B.p. 168-170° (2 mm), $n_D^{20}$ 1.4770, $d_4^{20}$ 0.98067, $MR_D$ 70.40, calculated 70.90.

N,N-(β,β'-Dichlorodiethyl)-β-(2-methylpyrrolidyl-1)-ethylamine dihydrochloride (X). Into a three-necked flask fitted with mechanical stirrer were charged 9 g of (VIII) and 45 ml of chloroform. ml of thionyl chloride in 15 ml of chloroform was gradually added dropwise, after which the mixture was kept at 45° for 2 hours. After the excess of thionyl chloride and the chloroform had been removed in vacuo, 12 g of oil was isolated. The latter crystallized after standing for many days in a vacuum-desiccator. The crystals were boiled with carbon and recrystallized from anhydrous methanol to give 8 g (61%) of the dihydrochloride of (X). M.p. 198-200°.

Found %: C 40.78, 40.75; H 7.54, 7.68. $C_{11}H_{24}N_2Cl_4$. Calculated %: C 40.48; H 7.41.

N,N-(β,β' Dichlorodipropyl)-β-(2-methylpyrrolidyl-1)-ethylamine (XI) dihydrochloride. Prepared on the same lines as (X) from 12.5 g of (IX) and 9 ml of thionyl chloride. Yield 24 g of (XI) in the form of an oil which did not crystallize even on prolonged standing.

Found %: C 43.62, 43.75; H 7.62, 7.56. $C_{13}H_{28}N_2Cl_4$. Calculated %: C 44.10; H 7.97.

## SUMMARY

Heating of a mixture of γ-acetopropyl alcohol and monoformylethylenediamine in presence of nickel gave 2-methyl-N-β-aminopyrrolidine (yield 60%) and 2,2-dimethylpyrrolidineethane (yield 10%).

A number of derivatives (at the amino group) of the first of the above compounds were prepared with the objective of study of their physiological activity.

## LITERATURE CITED

[1] A. P. Terent'ev and M. A. Volodina, Proc. Acad. Sci. USSR 88, 845 (1953).

[2] A. P. Terent'ev, M. A. Volodina and V. G. Mishina, J. Gen. Chem. 28, 223 (1958).*

[3] A. P. Terent'ev, M. A. Volodina, N. L. Podlesova and N. E. Golubeva, Proc. Acad. Sci. USSR 114, 1036 (1957).*

[4] L. Zechmeister and I. Truka, Ber. 63, 2883 (1930).

[5] I. L. Knuniants, G. V. Chelintsev and E. D. Osetrova, Proc. Acad. Sci. USSR 1, 312 (1934).

[6] R. Hansal, D. Vargason, and V. Hahn, Arhiv Kem. 27, 33 (1955).

[7] V. Hahn, R. Hansal, and D. Vargason, Arhiv Kem. 26, 21 (1954).

[8] Edward H. Lincoln, P. V. Heinzelman, and J. Hunter, J. Am. Chem. Soc. 71, 2902 (1949).

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*Original Russian pagination. See C.B. Translation.

# 4-NITRO-1,3-INDANEDIONE

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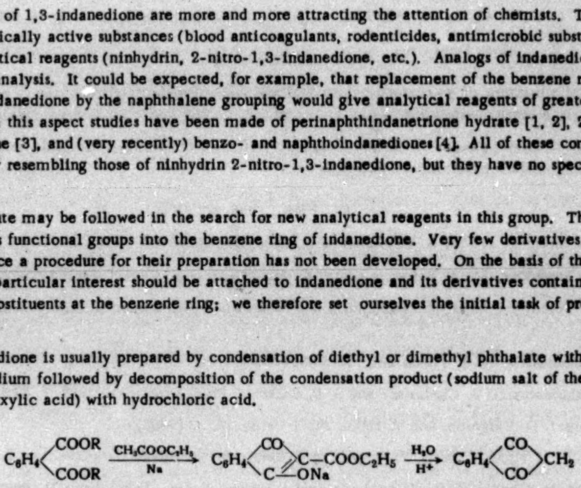
Derivatives of 1,3-indanedione are more and more attracting the attention of chemists. These derivatives include physiologically active substances (blood anticoagulants, rodenticides, antimicrobic substances) as well as valuable analytical reagents (ninhydrin, 2-nitro-1,3-indanedione, etc.). Analogs of indanedione are of particular interest in analysis. It could be expected, for example, that replacement of the benzene ring in ninhydrin or 2-nitro-1,3-indanedione by the naphthalene grouping would give analytical reagents of greater sensitivity or specificity. From this aspect studies have been made of perinaphthindanetrione hydrate [1, 2], 2-nitro-1,3-perinaphthindanetrione [3], and (very recently) benzo- and naphthoindanediones [4]. All of these compounds have properties broadly resembling those of ninhydrin 2-nitro-1,3-indanedione, but they have no special advantages over over the latter.

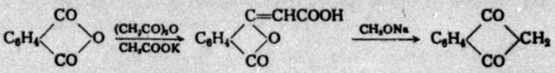
Another route may be followed in the search for new analytical reagents in this group. This is the introduction of various functional groups into the benzene ring of indanedione. Very few derivatives of this class are known as yet, since a procedure for their preparation has not been developed. On the basis of theoretical considerations [5,6] particular interest should be attached to indanedione and its derivatives containing negative (electrophilic) substituents at the benzene ring; we therefore set ourselves the initial task of preparing 4-nitro-1,3-indanedione.

1,3-Indanedione is usually prepared by condensation of diethyl or dimethyl phthalate with ethyl acetate in presence of sodium followed by decomposition of the condensation product (sodium salt of the ethyl ester of indanedionecarboxylic acid) with hydrochloric acid.



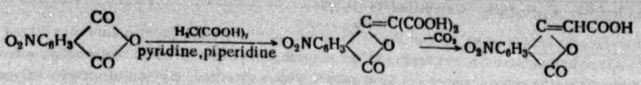
Preparation of a nitroindanedione with the nitro group in the benzene ring would necessitate starting from nitrophthalic acids, but we can at once predict that the nitro group would be lost in the above reaction. This proved to be the case.

A second route to indanedione is condensation of phthalic anhydride with acetic anhydride and isomerization of the resulting phthalylacetic acid to indanedione with the help of sodium methoxide.

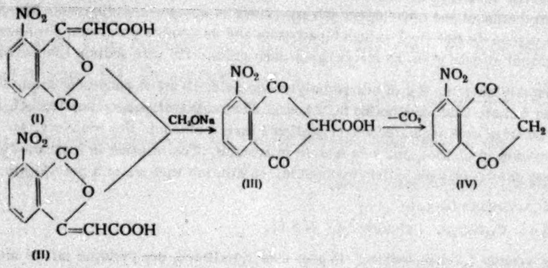


An attempt to prepare nitrophthalylacetic acid from 3-nitrophthalic anhydride was also unsuccessful (only resins were obtained).

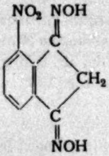
On replacing the acetic anhydride in the preceding reaction by malonic acid and performing the condensation in pyridine in presence of a few drops of piperidine, we were able to carry out the reaction at a lower temperature and to obtain nitrophthalylacetic acid.



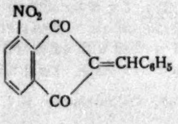
The prepared nitrophthalylacetic acid can theoretically exist in two isomeric forms (I and II). It is not yet certain which of them was obtained; this is not important for their further transformation into nitroindanedione, since rearrangement of either of the acids must give the same 4-nitro-1,3-indanedione (IV), as was confirmed experimentally.



The prepared 4-nitro-1,3-indanedione is a yellowish-grey, poorly crystallizing substance. It dissolves in alkalies with an orange-red color; on acidification it is recovered unchanged. It is poorly soluble in water; when heated with water or acetic acid, the solutions rapidly acquire a red-violet color. In all probability this is due to conversion of 4-nitro-1,3-indanedione into anhydro-bis-nitroindanedione or dinitribindone; this conversion evidently goes with greater facility than in the case of indanedione. The presence of two carbonyl groups in 4-nitro-1,3-indanedione was proved by preparation of the dioxime (V). The presence of an active methylene group was proved by formation of a condensation product with benzaldehyde (VI). Consequently, the correctness of formula (IV) for the prepared nitroindanedione is not in doubt.



(V)



(VI)

## EXPERIMENTAL

Pyridine salt of nitrophthalylacetic acid. 20 g of dry 3-nitrophthalic anhydride was dissolved by heating in 20 ml of freshly distilled pyridine and cooled to 40° (some of the anhydride came down). 10 drops of piperidine and 10 g of dry malonic acid were added. Carbon dioxide came off intensively and the precipitated anhydride gradually went into solution; fresh precipitate started to come down after a short time (its formation was promoted by stirring), and after 3 hours the whole of the mass was solid. The temperature was held at 35-40° during the whole period. After 5 hours the reaction came to an end. The product was 25-32 g (77-98%) of the pyridine salt of nitrophalylacetic acid possibly contaminated with the piperidine salt. This technical product was perfectly suitable for further working-up to 4-nitro-1,3-indanedione. The salt was soluble in water, methanol, ethanol, acetone and dioxane; insoluble in ether and chloroform. Aqueous solutions of the salt have an acid reaction, displace carbon dioxide from sodium bicarbonate and decolorize potassium permanganate solution. After crystallization from acetone, the light-yellow crystals of the salt had m.p. 128°.

Found %: N 8.94. $C_{15}H_{10}O_6N_2$. Calculated %: N 8.91.

Nitrophthalylacetic acid (I or II). 5 g of the pyridine salt of nitrophthalylacetic acid was mixed with 15 ml of sulfuric (1 : 5) or hydrochloric (8.3%) acid, and the solution was filtered. When the solution was allowed to stand, preferably while the sides of the vessel were rubbed with a glass rod, crystals of nitrophthalylacetic acid started to come down. The product was crystallized from 50% alcohol. The yellow crystals had m.p. 184° after recrystallization.

Found %: N 6.07, 5.89. $C_{10}H_5O_6N$. Calculated %: N 5.96

Nitrophthalylacetic acid is poorly soluble in ether and cold water, more easily soluble in hot water; it has good solubility in methanol and ethanol, and is very soluble in acetone and dioxane. The aqueous solutions intensively displace carbon dioxide from sodium bicarbonate and decolorize potassium permanganate solution. The solution in methanol at once gives an orange, gelatinous precipitate with sodium methoxide.

Methyl nitrophthalylacetate. 2 g of nitrophthalylacetic acid, 10 ml of anhydrous methyl alcohol and 6 drops of concentrated sulfuric acid were boiled for 3 hours. The methanol was evaporated off, the crystals of methyl nitrophthalylacetate were separated and crystallized from methanol; the white crystals with m.p. 98° were insoluble in water, soluble in alcohol, and very soluble in acetone. The solution in methanol gives a characteristic yellow-orange coloration with sodium methoxide; on dilution with water a precipitate of the same color comes down.

Found %: N 5.47. $C_{11}H_7O_6N$. Calculated %: N 5.62.

Sodium salt of 4-nitro-1,3-indanedione. 15 g of unrecrystallized, dry pyridine salt of nitrophthalylacetic acid was dissolved with gentle heating in 100 ml of methanol and to the cooled solution was added 2.2 g of sodium in 50 ml of anhydrous methanol in a fine jet with stirring. An orange-yellow solution and a gelatinous precipitate were formed. The mass stood for half an hour with occasional stirring, and the precipitate was collected and washed with methanol. Yield of sodium salt of 4-nitro-1,3-indanedione was 8.5 g (84%). An orange-yellow product was obtained after crystallization from aqueous alcohol; soluble in cold water and very much more soluble in hot water; poorly soluble in alcohol, insoluble in ether and chloroform. The aqueous solution of the salt loses its color on acidification and regains it when made alkaline. The solution turns red-violet when acidified with acetic acid; the color deepens on standing.

Found %: N 6.81, 6.41. $C_9H_4O_4NNa$. Calculated %: N 6.56.

4-Nitro-1,3-indanedione (IV). 5 g of the sodium salt of 4-nitro-1,3-indanedione was triturated in a mortar with 15 ml of dilute (1 : 5) sulfuric acid and remained standing for 30 minutes. The solid at first turned yellow and then gray. It was collected, washed with water and dried in the air, during which operation the 4-nitro-1,3-indanedione acquired a violet-brown shade. Yield 2.9 g (65%), m.p. 133°.

Found %: N 7.35, $C_9H_5O_4N$. Calculated %: N 7.33.

4-Nitro-1,3-indanedione is poorly soluble in cold water; on heating it froms a red-violet solution (dinitrobindone ?). Its solution in dioxane is yellow and the solutions in acetone and alcohols are violet-red. It is sparingly soluble in ether and insoluble in chloroform. It dissolves with an orange-red color in ammonia and in solutions of carbonates.

4-Nitro-1,3-indanedione dioxime (V). 0.2 g of 4-nitro-1,3-indanedione, 0.5 g of hydroxylamine hydrochloride and 0.5 g of sodium acetate in glacial acetic acid were boiled for 5 minutes. The precipitate was collected, washed with water and crystallized from alcohol. Brownish crystals which start to decompose at 210° without melting were formed.

Found %: N 19.22, $C_9H_7O_4N_3$. Calculated %: N 19.18.

2-Benzal-4-nitro-1,3-indanedione (VI). 0.2 g of 4-nitro-1,3-indanedione and 10 drops of benzaldehyde were heated for a short time on a water bath. The mass was boiled with alcohol and the residue of 2-benzal-4-nitro-1,3-indanedione was crystallized from ether. Fine, yellow crystals, m.p. 167° were formed.

Found %: N 5.02. $C_{16}H_9O_4N$. Calculated %: N 5.02.

## SUMMARY

Nitrophthalylacetic acid is formed by condensation of 3-nitrophthalic anhydride with malonic acid in pyridine in presence of piperidine. Its rearrangement in presence of sodium methoxide in methanol gives 4-nitro-1,3-indanedione which was characterized by preparation of the dioxime and benzal derivative.

## LITERATURE CITED

[1] R. Moubasher and W. Awad, J. Chem. Soc. 1949, 1137.

[2] R. Moubasher and A. Othman, J. Am. Chem. Soc. 72, 2666 (1950).

[3] E. Iu. Gudrinietse, E. Ia. Dreimanis and G. Ia. Vanag, J. Gen. Chem. 26, 272 (1956).*

[4] Meier and H. Lotter, Ber. 90, 222 (1957).

[5] I. M Korenman, Sci. Memoirs Gorkii State Univ. 17, 110 (1951).

[6] G. Vanag, Nitroindanedione (Acad. Sci. Latvian SSR Press, Riga, 1954), p. 116.

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*Original Russian pagination. See C.B. Translation.

# SYNTHESIS AND POLYCONDENSATION OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE

## III. INFLUENCE OF THE STRUCTURE OF THE SUBSTITUTING RADICAL ON THE DIRECTION OF ALKYLATION OF HEXAMETHYLENEDIAMINE

A. L. Klebanskii and M. S. Vilesova

We studied [1] the reductive alkylation of hexamethylenediamine in connection with the use of a series of carbonyl compounds containing radicals of different structures. This work established some relations between the structure of the radical of the carbonyl compound and its reactivity in alkylation. Formaldehyde occupies a special position in the series of carbonyl compounds employed.

It was impossible to perform the reaction with formaldehyde under the same conditions as for other aldehydes. Due to the high basicity of hexamethylenediamine, the added formaldehyde came down in the form of polymer, and hydrogenation was hindered. Alkylation was therefore conducted in a neutral medium, and the hexamethylenediamine was used in the form of the hydrochloride. With a diamine/aldehyde molar ratio of 1 : 2 the main product of reaction (yield about 75%) was unsymmetrical N-dimethylhexamethylenediamine with the formula $(CH_3)_2N-(CH_2)_6-NH_2$. A high-boiling fraction formed at the same time in small quantity contained mainly a trisubstituted diamine. Symmetrical N,N'-dimethylhexamethylenediamine and a monosubstituted derivative could not be detected among the reaction products.

Other methods of methylation of hexamethylenediamine were also tried, using the reactions of Hofmann [2] and Leuckart [3]. The Hofmann reaction with methyl iodide led to unsymmetrical N-dimethylhexamethylenediamine as the main product. The Leuckart reaction (involving reaction of an amine with formaldehyde in presence of formic acid followed by reduction with participation of formic acid) gave a methylation product identical with the products of the Hofmann reaction and of reductive methylation. The higher boiling fractions contained products approximating in composition to tri- and tetramethyl derivatives of hexamethylenediamine.

Consequently, the use of any of the above methods of methylation of hexamethylenediamine causes the second methyl group to enter the diamine molecule preferentially at the already methylated nitrogen (the second free amino group remaining untouched) with formation of unsymmetrical N-dimethylhexamethylenediamine. Even in presence of an excess of hexamethylenediamine a mono derivative is not formed. When the ethyl radical is introduced (in reductive alkylation) the main product (symmetrical N,N'-diethylhexamethylenediamine) is accompanied by a considerable quantity (20-30%) of the unsymmetrical N-disubstituted derivative. Introduction of n-propyl is accompanied by formation of a little unsymmetrical N-disubstituted derivative. Introduction of isopropyl and other higher radicals (n-butyl, isobutyl, unsymmetrical butyl) leads to symmetrical N,N'-disubstituted hexamethylenediamine as the predominant product (87-95% yield). An unsymmetrical disubstituted product could not be detected. The observed relations are summarized in Table 1.

The tendency of a second substituting methyl radical to attach itself preferentially at an already substituted group and not at the free amino group of the diamine is presumably due to the increased susceptibility to coordination of the unshared electron pair at the nitrogen as the result of shift of the electron density under the influence of the positive inductive effect of the substituent. The direction of the reaction depends, however, in great measure also on the size and spatial structure of the groups.

TABLE 1

Influence of the Structure of the Alkylating Compound on the Direction of N,N'-dialkylation of Hexamethylenediamine

| Alkylating compound | Yield on basis of reacted hexamethylenediamine (in %) | |
|---|---|---|
| | symmetrical N,N'-dialkyl derivative | unsymmetrical N-dialkyl derivative |
| Formaldehyde | Not detected | 72 |
| Acetaldehyde | 40 | 20 |
| Propionaldehyde | 58 | 2 |
| Acetone | 93 | Not detected |
| Butyraldehyde | 85 | The same |
| Methyl ethyl ketone | 90 | ″ ″ |

The steric hindrance created by the methyl group is insignificant, and the directivity of disubstitution at the one $NH_2$ group is governed by the enhancement of activity of the amino group under the influence of the positive inductive effect of the substituent. When an ethyl group is introduced the enhancement of reactivity of the amino group under the influence of a substituent is already lowered to a certain degree by the increasing steric effect caused by the ethyl being larger than the methyl. Starting from isopropyl, the shielding effect acquires a dominating influence and governs the preferential directivity towards N,N'-disubstitution.

Preliminary experiments on the introduction of tert.butyl and trimethylsilyl into the amino group of hexamethylenediamine (using the Hofmann reaction) were undertaken with the aim of preparing N-alkylated hexamethylenediamines with highly branched substitutuents. The experiments showed that tert.butyl cannot be introduced under the experimental conditions. Trimethylsilyl easily replaces the 2 hydrogen atoms in each of the amino groups to give preferentially a tetrasubstituted diamine. This difference in alkylation behavior is evidiently due to the strong shielding of the central carbon atom in tert.butyl, whereas the steric influence does not prevent interaction of trimethylsilyl with the nitrogen of the amino group because the atomic radius of silicon (1.17 A) is much larger than that of carbon (0.77 A).

## EXPERIMENTAL

Reductive methylation of hexamethylenediamine – Into a autoclave (for reduction procedure see [1]) were charged a solution of 17.45 g of hexamethylenediamine in 30 ml of alcohol neutralized with 37.5 ml of concentrated hydrochloric acid, 9.0 g of formaldehyde (in the form of 29 ml of 37% formalin) and 0.2 g of platinum oxide. The diamine/aldehyde molar ratio was 1 : 2. Absorption of hydrogen at room temperature was observed for 40 minutes. The pressure dropped from 102 to 19 atm , corresponding to 320 millimoles of hydrogen (100% of the theoretical quantity). After the catalyst had settled, the mixture was decanted and the diamine displaced from the salt with 150 ml of 70% NaOH; it was dried over potassium carbonate and vacuum-fractionated in a nitrogen atmosphere. The vapor temperature quickly rose to 67-68° (2 mm) and the greater portion of the product came over in this range. The vapor temperature then rose steadily from 69 to 120° (2 mm) (a second fraction was collected). The quantity of still residue was insignificant. The main fraction – 67-68° (2 mm) – weighed 16.1 g (yield 75% on the diamine taken into reaction) and consisted of unsymmetrical N-dimethylhexamethylenediamine, as evident from the analytical results.

B.p. 67-68° 2 mm, $d_4^{25}$ 0.831, $n_D^{25}$ 1.447, $MR_D$ 45.9; calculated 46.3.

Found %: N (total) 19.4; $NH_2$ 9.6[*], M (Rast method) 150. $C_8H_{20}N_2$. Calculated %: N 19.4; $NH_2$ 9.7; M 14 4.

Judging by the content of total nitrogen (16.8%) the 69-120° (2 mm) fraction is a mixture of tri- and tetramethyl substituted derivatives with nitrogen contents of 17.7 and 16.3%.

Reductive ethylation of hexamethylenediamine. A solution of 11.6 g of hexamethylenediamine in 67 ml of alcohol, 8.8 g of acetaldehyde (diamine/aldehyde molar ratio 1 : 2) and 0.2 g of platinum oxide were charged into a metal ampoule cooled to −8 to −10°. The aldehyde was added in a hydrogen atmosphere. Absorption of hydrogen was observed for 30 minutes. The pressure dropped from 110 to 61 atm., corresponding to 254 millimoles of hydrogen (100% of the theoretical quantity). After the settling of the catalyst, the solvent was distilled off; the residue was dissolved in ether, dried over potassium carbonate, and (after removal of the ether) fractionated in vacuo in a nitrogen medium. The first fraction came over at 67-98° (5 mm) and contained a considerable quantity of hexamethylenediamine (total nitrogen content 21.3%). A second fraction was collected at 98-105° (5-7 mm) and its nitrogen content (16.2%) corresponded to the diethyl derivative of hexamethylenediamine. The higher boiling products coming over at 106-205° (5 mm) contained more highly alkylated derivatives (nitrogen content 13.7%).

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[*] The percentage of $NH_2$ was determined by the Van Slyke method and expressed as percentage of N.

The 98-105° (5-7 mm) fraction was analyzed for its content of $NH_2$ groups (found 1.9% calculated as nitrogen). The result corresponded to a mixture of 76% of symmetrical N,N'-diethylhexamethylenediamine and 24% of unsymmetrical N-diethylhexamethylenediamine. A second fractionation gave a narrower cut at 101-105° (5-7 mm) which contained 96% of the symmetrical derivative. Analytical data and yields are listed in [1]. The latter publication also describes the synthesis of N,N'-diisopropyl and N,N'-di-n-butyl derivatives of hexamethylenediamine.

Alkylation of hexamethylenediamine with tert. butyl chloride or bromide. Experiments were at first performed in a flask with a reflux condenser and stirrer. 11.6 g of diamine was reacted with 18.5 g of tert. butyl chloride; the reaction was carried out both with and without a solvent (dioxane and pyridine, each in quantity of 30 ml). The duration of the reaction was 2-2.5 hours at a bath temperature of 100-125°. A weighed sample was dissolved in methanol and neutralized with HCl (1 : 1); the methanol was evaporated off and the residue dissolved in water. The solution was analyzed for its content of $NH_2$ groups by the Van Slyke method. The amount of unreacted diamine was 97.8-98.4% of the original quantity.

Experiments on alkylation in sealed glass ampoules were also run in which 4.62 g of tert. butyl chloride or 6.85 g of tert. butyl bromide was added to 2.90 g of hexamethylenediamine. The ampoules were kept at 100° for 48 hours. With progressive heating the separation of a crystalline material was observed. When the ampoules were opened, 70 and 96 ml of gas respectively were evolved (evidently isobutylene). Analysis of the mixtures for the $NH_2$ group showed that the quantities of unsubstituted diamine were respectively 99.0 and 99.2% of the original quantities.

Introduction of trimethylsilyl. Experiments were run at first in a flask with a reflux condenser and stirrer. 28.4 g of trimethylchlorosilane was added gradually to a solution of 14.5 g of hexamethylenediamine in 30 ml of anhydrous pyridine (the apparatus was shielded against access of moisture from the air by means of calcium chloride tubes). Reaction was effected at 125° for 4 hours. The reaction mixture, in which a gelatinous precipitate appeared, was repeatedly extracted with ether. After the ether and pyridine had been distilled off, the residue was fractionally distilled in vacuo in a nitrogen atmosphere. Nearly the whole of the product came over at 150-165° (2 mm). Analytical results are presented in Table 2.

TABLE 2

Analyses of Fractions of Silico Derivatives of Hexamethylenediamine

| Boiling point (pressure in mm) | Weight (in g) | Content (in %) of | | Theoretical N content (in %) | |
|---|---|---|---|---|---|
| | | N (by titration | $NH_2$ group (Van Slyke techn.) | trisubstituted | tetrasubstituted |
| 150—165° (2) . . . . . | 4.8 | 7.4 | 7.2 | 8.4 | 7.0 |
| 153—170 (2) . . . . . . | 2.3 | 7.8 | 7.8 | | |

The tabulated data show that the prepared compounds approximate in composition to tri- and tetra substituted derivatives, and the N – Si bond is broken under the conditions of the Van Slyke determination.

## SUMMARY

1. It is shown that the preferred course of the reductive alkylation of hexamethylenediamine which is in the direction of symmetrical N,N'-dialkylation is governed by two opposing influences; the enhanced reactivity of the substituted amino group and the steric effect of the substituent.

2. It was established that the reaction goes exclusively in the direction of symmetrical N,N'-disubstituted derivatives when the alkylating radical is isopropyl or higher.

3. Difficulties are encountered in obtaining the pure symmetrical derivative of hexamethylenediamine when introducing the ethyl and n-propyl radicals. When the methyl radical is introduced the reaction is wholly directed towards formation of the unsymmetrical substitution product.

4. It is shown that the tert.butyl group could not be introduced into the amino group of hexamethylenediamine under the conditions of reaction, whereas trimethylsilyl easily substitutes both of the hydrogen atoms with formation of a tetrasubstituted derivative. This difference in behavior is explained by the difference in the steric effects of the two types of groups due to the difference in atomic radii of silicon and carbon.

## LITERATURE CITED

[1] A. L. Klebanskii and M. S. Vilesova, J. Gen. Chem. 28, 1066, 1073 (1958).*

[2] J. Houben, Methods of Synthesis of Organic Compounds [in Russian] (1949), Vol. 4, Part 1, Book 1, p. 446.

[3] Synthetic Organic Preparations [in Russian], Collection, Vol. 3, 452 (1952)

Received May 25, 1957.

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*See C.B. Translation.

# SYNTHESIS OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE AND THEIR POLYCONDENSATION

## V. SOME PROBLEMS OF THE KINETICS OF THE REDUCTIVE ALKYLATION OF HEXAMETHYLENEDIAMINE

A. L. Klebanskii and M. S. Vilesova

A. Dependence of the reaction velocity on the reaction conditions. Results obtained in a study of the synthesis of N-substituted diamines, as well as special experiments, permitted calculations with the objective of determination of the reaction order and allowed the comparison of the relative reaction rates with different alkylating compounds.

A study of the reductive alkylation of hexamethylenediamine with aldehydes and ketones both at high (100-50 atm pressure and at atmospheric pressure showed that the reaction is of zero order. This order is evidently determined by sorption which is limited by the step of diffusion of the reactants from the solution to the catalyst. It was shown that the reaction rate does not depend on the concentration of the components and on their change during the reaction. Results are plotted in Figs. 1-5.

Study of reductive alkylation under pressure of 40-10 atm revealed a nonlinear dependence of the reaction rate on time, as we see from Figs. 6 and 7. Calculation showed that the reaction under these conditions is approximately first order in dependence on the pressure and consequently also on the hydrogen concentration in the liquid phase. The velocity constants of this reaction, in dependence on the quantity of absorbed hydrogen, are calculated from the equation for a first-order reaction (Table 1).

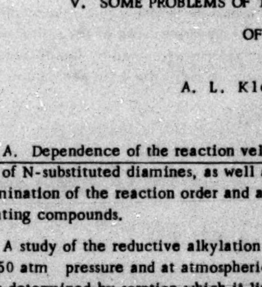

Fig. 1. Reduction of a mixture of hexamethylenediamine and carbonyl compound in the 100-50 atm pressure range. 1) propionaldehyde, 2) acetone, 3) methylethyl ketone, 4) butyraldehyde.

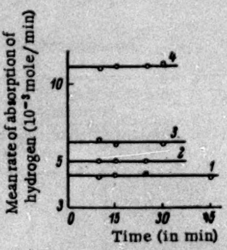

Fig. 2. Mean rate of absorption of hydrogen (according to Fig. 1) at 100-50 atm 1) propiondehyde, 2) acetone, 3) methyethyl ketone, 4) butyraldehyde

The observed difference in the course of reductive alkylation in different pressure regions in respect of reaction order may be explained in the following manner. During reduction at atmospheric pressure the pressure remains constant throughout the whole of the reaction period and has no influence on the reaction velocity

**TABLE 1**

Velocity Constants of the Reductive Alkylation of Hexamethylenediamine (in respect of hydrogen). P = 4-10 atm., Temperature 25°

| Reaction time (min) | Alkylating compound | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | acetone | | methyl ethyl ketone | | propional-dehyde | | n-butyral-dehyde | |
| | $K \cdot 10^{3}$ | percentage transf. | $K \cdot 10^{3}$ | percentage transf. | $K \cdot 10^{3}$ | percentage transf. | $K \cdot 10^{3}$ | percentage transf. |
| 2.5 | 3.20 | 28 | 2.36 | 21 | 1.84 | 17 | 1.32 | 12 |
| 5.0 | 3.44 | 54 | 2.50 | 42 | 1.92 | 33 | 1.40 | 24 |
| 7.5 | 3.22 | 70 | 2.45 | 56 | 1.88 | 46 | 1.39 | 36 |
| 10.0 | — | — | 2.23 | 66 | 1.76 | 55 | 1.26 | 42 |

During reduction in the 100-50 atm. pressure range there is evidently complete sorptive saturation of the catalyst with hydrogen even at the lower pressure limit, and change of pressure exerts no influence on the rate of reductive alkylation. Reduction of the hexamethylenediamine–carbonyl compound mixture at 40-10 atm is associated with absence of complete saturation of the catalyst with hydrogen, and the degree of saturation evidently depends on the magnitude of the pressure. The first-order reaction is determined in this case by the falling hydrogen pressure during the reaction.

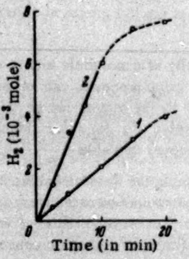

Fig. 3. Reduction of a mixture of hexamethylenediamine and carbonyl compound at atmospheric pressure (degree of conversion approx. 75% . 1) acetone, 2) butyraldehyde

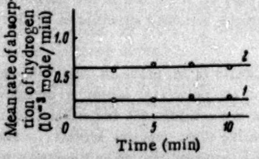

Fig. 4. Mean rate of absorption of hydrogen (according to Fig. 3) at pressure of 760 mm. 1) acetone, 2) butyraldehyde

B. Influence of the structure of the alkylating compound on the velocity of reductive alkylation of hexamethylenediamine. The reaction rate is markedly dependent on the structure of the alkylating aldehyde or ketone. Data for reduction under pressure are plotted in Fig. 8. The rate of this reaction is determined by the rate of chemisorption of the starting components on the catalyst. In the cases in question, where the diamine is always the same substance, the factor governing the character of the reaction is the structure of the alkylating carbonyl compound.

An insight into the influence of structure of the carbonyl compound on the reaction rate during reductive

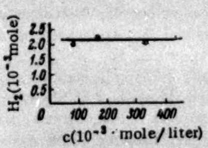

Fig. 5. Dependence of quantity of absorbed hydrogen (in reduction of a mixture of hexamethylene diamine and butyraldehyde) on the initial concentration of reactants (after 20 minutes).

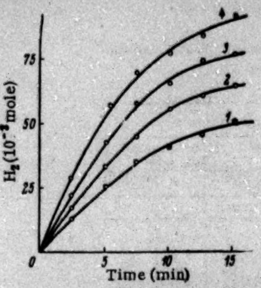

Fig. 6. Reduction of a mixture of hexamethylenediamine and carbonyl compound in the pressure range of 40-10 atm. 1) butyraldehyde, 2) propionaldehyde 3) methyethyl ketone, 4) acetone.

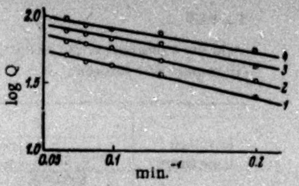

Fig. 7. Dependence of the logarithm of the quantity of absorbed hydrogen (Q in mole · $10^{-2}$) on the reciprocal of the time. 1) butyraldehyde, 2) propionaldehyde, 3) methylethyl ketone, 4) acetone.

alkylation is obtained from Table 2 which lists the velocity constants with different alkylating agents (calculated with respect to hydrogen at 25°).

The influence of the structure of the carbonyl compound on the course of reductive alkylation (determined by the rate of chemisorption) is evidently associated with the change of the polarization of the C = O bond in dependence on the character of the aliphatic radicals linked with the carbonyl. In presence of methyl groups the electron density is inductively shifted to the oxygen and this increases its electronegative character and in turn the polarizability of the $C^{+}-O^{-}$ bond. The number of methyl groups and their distance from the carbonyl determine the degree of this polarization.

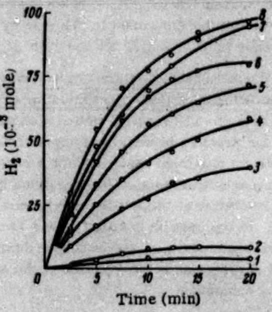

Fig. 8. Dependence of the rate of reductive alkylation on the structure of the alkylating compound. 1) diisopropyl ketone, 2) diisobutyl ketone, 3) isobutyraldehyde, 4) n-butyraldehyde, 5) propionaldehyde, 6) methylethyl ketone, 7) acetaldehyde. 8) acetone.

The polarity of a molecule and in turn its activity in chemisorption processes can be quantitatively characterized by the magnitude of the dielectric constant. The value of ε for some aldehydes and ketones are presented in Table 3.

On comparing the data of Tables 2 and 3 we see that carbonyl compounds are arranged in the same order in respect of magnitudes of velocity constants and magnitudes of dielectric constants. Although values of ε could not be found in the literature for isobutyraldehyde, we can assume that the branched structure and the presence of two methyl groups must cause the polarization of the C = O bond to be greater than in n-butyraldehyde. Experiments show, however, that alkylation with isobutyraldehyde proceeds more slowly than with n-butyraldehyde. This effect may be attributed to the steric hindrance arising from the branched structure of the iso compound.

The steric factor plays an important part in all of the cases of alkylation in question and depresses the influence of the polarizing factor, as demonstrated in particular in the alkylation with highly branched ketones (which have a considerable inductive effect). It does not appear possible in the present work to quantitatively characterize these opposing effects (increase of polarization and intensification of the steric effect) by the process of chemisorption. It only remains to note that when highly branched radicals are introduced (by alkylation with the help of diisopropyl and diisobutyl ketones) the screening effect definitely predominates, and this is reflected in the exceptional slowness of the reaction even at higher temperature, notwithstanding that the polar effect must here be considerable.

TABLE 2

Velocity Constants of the Reductive Alkylation of Hexamethylenediamine with Various Aldehydes and Ketones

| Alkylating compound | $K_{mean} \cdot 10^2$ (with respect of hydrogen |
|---|---|
| Acetone . . . . . . . | 3.29 |
| Acetaldehyde | 2.81 |
| Methyl ethyl ketone . | 2.38 |
| Propionaldehyde . . . | 1.85 |
| n-Butyralde | 1.34 |
| Isobutyraldehyde . . . . . . . | 0.86 |
| Diisobutyl ketone . . | 0.24 |

TABLE 3

Dielectric Constants of Aldehydes and Ketones [1, 2]

| Carbonyl compound | $\epsilon$ | Temperature |
|---|---|---|
| Acetone . . . . . | 21.4 | 20° |
| Acetaldehyde | 22.2 * | 10 |
| Methyl ethyl ketone . | 18.0 | 20 |
| n-Butyraldehyde | 13.8 | 26 |

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* The value of $\epsilon$ falls with rising temperature, and for acetaldehyde at 20° it will evidently be lower than for acetone

Consequently, the velocity of reductive alkylation of hexamethylenediamine in depending on the structure of the carbonyl compound is determined by two opposing influences: the polarizing effect of the substituting radical on the C = O group on the one hand, and the steric factor on the other hand. Polarization plays the predominant part in the case of lower aldehydes and ketones whose steric effect is insignificant, while the screening effect is more powerful in the case of higher members of the series with highly branched structures.

## EXPERIMENTAL

Reductive alkylation of hexamethylenediamine at atmospheric pressure. Experiments were performed in a Willstatter hydrogenation vessel of 100 ml capacity which was attached to a shaking machine and immersed in a thermostat whose temperature was kept constant to within 0.3° with the help of a contact thermometer and an electronic relay. A weighed amount of catalyst in alcohol was placed in the vessel (in the thermostat) connected to a gas buret filled with hydrogen (supplied from a gasholder) and purged with 4 volumes of hydrogen. The shaking machine was then started, the hydrogenation vessel was linked with the buret and the platinum oxide was reduced to platinum black. The latter was saturated with hydrogen until no more gas was absorbed. A small beaker containing a weighed quantity of the carbonyl compound was suspended from a movable piston pushed through the stopper. The weighed sample of hexamethylenediamine in alcohol was placed directly in the hydrogenation vessel which was again purged with 4 volumes of hydrogen. The piston was then pushed down in a hydrogen atmosphere and the beaker with the carbonyl compound fell into the hexamethylenediamine solution. At that instant the shaking machine was set in motion and measurement was made of the quantity of hydrogen (in ml) absorbed in unit time (the time was measured with a stopwatch). The progress of the reaction was followed from the volume of $H_2$ absorbed. A preliminary determination had been made of the number of shakings required for the process to proceed in the kinetic region (320 per minute).

Experiment 1. To a solution of 0.464 g of hexamethylenediamine in 23.4 ml of alcohol were added 0.576 g of butyraldehyde and 0.2 g of platinum oxide. The reaction was conducted at 20°. Data for hydrogen absorption are plotted in Fig. 3.

Experiment 2. To a solution of 0.232 g of hexamethylenediamine in 24.4 ml of alcohol were added 0.232 g of acetone and 0.05 g of platinum oxide. Reaction was conducted at 16°. Data for hydrogen absorption are plotted in Fig. 3.

Experiment 3. To solutions of 0.232 g of hexamethylenediamine in 24.4 ml of alcohol, 0.464 g in 24.0 ml of alcohol and 0.961 g in 22.6 ml of alcohol were added, respectively, 0.288, 0.576 and 1.193 g of butyraldehyde and 0.050 g of platinum oxide. The total volume in each case was kept at 25.0 ml, while the concentrations of diamine in moles/liter × $10^3$ were 80, 160 and 134. Reaction was performed at 25°. Data for the hydrogen absorption are plotted in Fig. 5.

Study of the dependence of the rate of reductive alkylation on the structure of the alkylating agent. Experiments were performed under pressure in the autoclave described earlier [3]. Constant conditions that would facilitate comparison of individual experiments were established by the provision of the autoclave with a metal jacket through which water was circulated from an ultrathermostat. Constancy of temperature inside the autoclave (30 ± 0.2°) was checked by a thermocouple in a pocket (sensitivity 0.2°). A 60-atm. pressure gage graduated in atmospheres enabled the pressure drop to be recorded to an accuracy of 0.25 atm. The volume of the reaction mixture and the initial pressure were kept strictly constant in all of the experiments. In each case the number of shakings was 280 per minute. Into the autoclave were charged the solution of the weighed sample of hexamethylenediamine in alcohol, the catalyst and the alkylating agent (the latter in a thin-walled sealed glass ampoule containing an internal sharp-tipped projection). As already indicated, the autoclave was purged with hydrogen, the necessary pressure was established, and the autoclave was placed on the shaking machine and thermostated for 20 minutes. The shaking machinism was then put in motion, the glass ampoule broke immediately (as reflected in commencement of pressure drop), and the components were mixed in a hydrogen atmosphere. The pressure drop was recorded by the gage and the duration was noted by stopwatch.

The amounts of carbonyl compound taken for 5.80 g of hexamethylenediamine were 4.40 g of acetaldehyde, 5.80 g of propionaldehyde or acetone, 7.20 g of n-butyraldehyde, isobutyraldehyde or methylethyl ketone, 11.40 g of diisopropyl ketone, and 14.20 g of diisobutyl ketone. The volume of the mixture was made up to 45 ml (roughly) by addition of alcohol. In each case the quantity of platinum oxide was 0.05 g, and the initial pressure was 40 atm. Data for hydrogen absorption are plotted in Figs. 6 and 8. The velocity constants of the respective reactions were calculated from these data.

Determination of the reaction order in reductive alkylation of hexamethylenediamine at above 50 atm. Experiments were performed in the autoclave under the previously described conditions.*

Experiment 1. 17.40 g of hexamethylenediamine in 51 ml of alcohol was treated with 17.40 g of propionaldehyde and 0.05 g of platinum oxide. Initial pressure 126 atm.

Experiment 2. 11.6 g of hexamethylenediamine in 19.0 ml of alcohol was treated with 11.6 g of acetone and 0.05 g of platinum oxide. Initial pressure 98 atm.

Experiment 3. 29.0 g of hexamethylenediamine in 17.0 ml of alcohol was reacted with 36.0 g of n-butyraldehyde in presence of 0.20 g of platinum oxide. Initial pressure 130 atm.

Experiment 4. 17.0 g of hexamethylenediamine in 46.0 ml of alcohol was reacted with 36.0 g of methylethyl ketone in presence of 0.10 g of platinum oxide. Initial pressure 96 atm.

The course of hydrogen absorption is plotted in Fig. 1.

## SUMMARY

1. It was established that the reductive alkylation of hexamethylenediamine at normal pressure and at pressures about 50 atm. is a reaction of zero order; in the 10-40 atm. pressure range it is a first-order reaction. The difference in behavior is due to incomplete sorptive saturation of the catalyst in the 10-40-atm. range.

2. It was shown that the rate of reductive alkylation of hexamethylenediamine is determined by the relative polarity of the alkylating compounds on the one hand and by the steric influence of their structure on the other hand. The second factor plays a predominant part only in the case of higher carbonyl compounds with considerable branching.

## LITERATURE CITED

[1] Handbook of Chemistry [in Russian] (State Sci.-Tech. Chem. Lit. Press, 1951), Vol. 1.

[2] Handbook of Chemistry and Physics (1951-1952, 33rd ed. p. 2109.

[3] A. L Klebanskii and M. S. Vilesova, J. Gen. Chem., 28, 1066 (1958).**

Received May 25, 1957.

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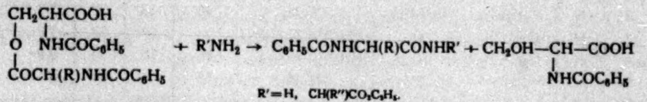
* The 60-atm. pressure gauge was replaced by a 250-atm. gauge.

** See C.B. Translation.

# THE FERMENTATIVE SYNTHESIS OF N-PEPTIDES FROM O-PEPTIDES OF β-HYDROXYAMINO ACIDS

M. M. Botvinik and S. M. Avaeva

In a study of the specific properties of N-peptides of serine and threonine, we showed [1] that they are susceptible not only to intramolecular but also to intermolecular rearrangement. The reaction goes according to the equation



$$\begin{matrix}CH_2CHCOOH\\ |\qquad|\qquad\\ O\quad NHCOC_6H_5\\ |\qquad\qquad\qquad\\ COCH(R)NHCOC_6H_5\end{matrix} + R'NH_2 \rightarrow C_6H_5CONHCH(R)CONHR' + CH_2OH-\underset{\displaystyle NHCOC_6H_5}{\underset{|}{CH}}-COOH$$

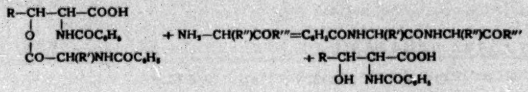
$R' = H,\ CH(R'')CO_2C_2H_5.$

When O-peptides of N-benzoylserine and threonine are reacted with ammonia, the reaction is nearly instantaneous, but with esters of amino acids and peptides, the process is slow at elevated temperatures and the yield is poor. If, however, the reaction is performed in presence of chymotrypsin, it goes with great facility and leads to derivatives of peptides of the L-series [2]. It seemed to us that this reaction, in which O-peptides of β-hydroxamino acids are carriers of amino acid residues in the fermentative synthesis of peptides, is of interest in connection with possible secondary reactions in nature. In the present work we investigated a number of other substances from this aspect. Experiments were run with N-benzoyl-O-benzoylphenyl-alanyl-serine, N-benzoyl-O-benzoylglycyl-serine and N-benzoyl-O-benzoylphenylalanyl-threonine. Acceptors for the acylamino acid residues were the ethyl esters of glycine, phenylalanine, glycylglycine and leucylglycine. All of the starting compounds were racemic, and in all cases the optically active peptides were obtained. Results of the investigations are set forth in the table. Experiments were performed at room temperature and at a pH of 7.8-8. The reaction went with particular ease when using N-benzoyl-O-benzoylphenylalanylserine which reacted with esters of glycine, phenylalanine, glycylglycine and leucylglycine in the course of 10-30 minutes. Precipitation of the esters of the benzoylpeptides was completed within this period (see experiments 1-4). The yield of the latter was 46-68%. The experiment with N-benzoyl-O-benzoylphenylalanylthreonine went in similar fashion, although the yield of peptide ester was only 26% (experiment 6). No precipitate was formed in reactions of N-benzoyl-O-hippurylserine with the ethyl ester of glycine; the reaction was therefore run for 48 hours, and inspissation of the solution led to separation of 15% of the ester of benzoylglycylglycine (experiment 5). Change of reaction conditions had little influence on the synthesis of peptides. Rise of temperature to 34° shortened the process, but change of pH to 8.5 had no appreciable effect.

Preliminary experiments were run with N-benzoyl-O-hippurylserine and N-benzoyl-O-benzoylvalylserine, using esters of phenylalanine, glycylglycine and leucylglycine as acceptors of amino acid residues. These experiments gave unsatisfactory results. The reason was evidently not the hydrolysis of the O-peptide by chymotrypsin since the same N-benzoyl-O-peptides of serine that had not reacted with amino acid esters were not split by the ferment. Experiments on hydrolysis of N-benzoyl-O-peptides of serine showed that N-benzoyl-O-benzoylphenylalanylserine is hydrolyzed to the extent of 10% in 10 minutes by chymotrypsin under selected conditions, while N-benzoyl-O-benzoylvalylserine and N-benzoyl-O-benzoylglycylserine are not altered in 90 minutes (see diagram. These facts may be evidence in support of the theory [3] that both of the processes –

synthesis and hydrolysis of peptides – proceed via the same intermediate compound, which is formed by the amino acid residue and the ferment.

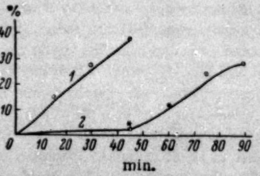
Summary of Fermentative Syntheses



$$\underset{\underset{\text{CO}-\text{CH(R')NHCOC}_6\text{H}_5}{|}}{\underset{\text{O}}{|}}\!\!\!\!\text{R}-\text{CH}-\underset{\text{NHCOC}_6\text{H}_5}{\underset{|}{\text{CH}}}-\text{COOH} + \text{NH}_2-\text{CH(R'')COR'''} = \text{C}_6\text{H}_5\text{CONHCH(R')CONHCH(R'')COR'''} + \text{R}-\underset{\text{OH}}{\underset{|}{\text{CH}}}-\underset{\text{NHCOC}_6\text{H}_5}{\underset{|}{\text{CH}}}-\text{COOH}$$

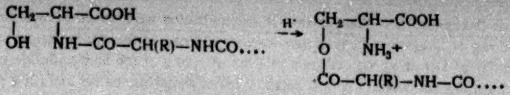
| Expt. No. | First component | | Second component | | Yield of peptide ester (in %) | Reaction conditions | | |
|---|---|---|---|---|---|---|---|---|
| | R | R' | R'' | R''' | | time (min) | temp. | pH |
| 1 | H | $C_6H_5CH_2$ | H | $OC_2H_5$ | 48 | 10 | 20° | 8.1 |
| 2 | H | $C_6H_5CH_2$ | $C_6H_5CH_2$ | $OC_2H_5$ | 46 | 10 | 20 | 7.8 |
| 3 | H | $C_6H_5CH_2$ | H | $NHCH_2CO_2C_2H_5$ | + | 30 | 20 | 7.8 |
| 4 | H | $C_6H_5CH_2$ | iso -$C_4H_9$ | $NHCH_2CO_2C_2H_5$ | 68 | 10 | 20 | 7.8 |
| 5 | H | H | H | $OC_2H_5$ | 15 | 48 hours | 20 | 8 |
| 6[2] | $CH_3$ | $C_6H_5CH_2$ | H | $OC_2H_5$ | 26 | 10 | 20 | 7.8 |

The ability of esters of amino acids to form peptides under the influence of chymotrypsin was discovered by Brenner and co-workers [4]. They showed that, in presence of chymotrypsin, esters of methionine and threonine form a mixture of peptides, their esters and amino acids. The reaction proceeded for 20-40 hours at 22-38° and a pH of 9. Tauber [5] found that at pH 8.8 and 37° the ethyl ester of phenylalanine, to whose solution chymotrypsin had been added, forms a peptide ester. The latter begins to come down after 10 minutes. Its yield was 10%. I. L. Kaganova and V. N Orekhovich [6] studied this reaction in the case of the ethyl ester of threonine at pH 9, a temperature of 37° and an experimental period of 10 minutes to 2 hours. They found that the reaction is selective: the ethyl ester of tyrosine reacted with glutamine, asparagine, leucylglycine, glycylglycine, etc., but not with aspartic acid, glutamic acid, glycyltryptophan, glycine and leucine. Lestrovaia and Mardashev [7] found that the ethyl ester and the amide of phenylalanine behave even more selectively. A large number of diverse amino acids and peptides were investigated, and phenylalanine was found to react only with itself.



Hydrolysis of N-benzoyl-O-benzoylphenylalanylserine by chymotrypsin. 1) experiment with ferment, 2) experiment without ferment (• denotes point of addition of ferment).

The investigations that we undertook are different from those described in the literature. Experiments were performed with esters of amino acids in which the alcoholic residue was a β-hydroxyamino acid, i.e., the compounds under investigation more closely resembled natural substances. The esters used were not those of amino acids themselves but of their benzoyl derivatives, so that the reaction stopped at the dipeptide stage. The reaction required a shorter period of time at a lower pH and with a smaller quantity of ferment. In our opinion the reactions in question are not devoid of interest if only because O-peptides of β-hydroxyamino acids are formed with relative ease from N-peptides of β-hydroxyamino acids in an acid medium according to the equation [8]:



$$\underset{OH}{CH_2}-\underset{NH-CO-CH(R)-NHCO\ldots}{CH}-COOH \xrightarrow{H^{\cdot}} \underset{\underset{CO-CH(R)-NH-CO\ldots}{O}}{CH_2}-\underset{NH_3^+}{CH}-COOH$$

## EXPERIMENTAL

1. Reaction of O-benzoyl-D,L-phenylalanyl-N-benzoyl-D,L-serine with the ethyl ester of glycine. a) In presence of chymotrypsin. 500 mg of O-benzoylphenylalanyl-N-benzoylserine was dissolved in hot alcohol, neutralized with 1 N sodium hydroxide and mixed in presence of 2 ml of phosphate buffer (pH 7.9) with a solution of 700 mg of the hydrochloride of the ethyl ester of glycine in the equivalent quantity of 1 N caustic alkali. To the reaction mixture was added 3-5 mg of chymotrypsin. The experiment was performed at a pH of 8.1. After a few minutes, long needles started to come down. After 8-10 minutes the precipitate was filtered and recrystallized from aqueous alcohol. The ethyl ester of benzoyl-L-phenylalanylglycine had m.p. 148-149°. Its yield was 24% calculated on the racemate and 48% on the L-antipode of the ester of phenylalanine [2].

Found %: C 67.76; H 6.42; N 7.92. $C_{20}H_{22}O_4N_2$. Calculated % : C 67.70; H 6.21; N 7.92.

After the mother liquor had stood for a long period or after a fresh portion of chymotrypsin had been added to it, no separation of the ethyl ester of benzoylphenylalanylglycine was observed.

b) Blank experiment without ferment. 400 mg of O-benzoylphenylalanyl-N-benzoyl serine was dissolved in hot alcohol, neutralized with 1 N solution of caustic alkali and mixed in presence of 2 ml of phosphate buffer (pH 7.9) with a solution of 500 mg of the hydrochloride of the ethyl ester of glycine in the equivalent quantity of alkali. The pH of the solution was brought to 8.1. The slightly cloudy solution did not change in the course of several hours. After 18 hours the salt of O-benzoylphenylalanyl-N-benzoylserine and the ethyl ester of glycine was isolated. M.p. 147-148°. The salt is easily soluble in water and gives a positive ninhydrin reaction. The result of the Van Slyke nitrogen determination is given below.

Found %: $NH_2$ 2.52. Calculated %: $NH_2$ 2.48.

c) In presence of diisopropyl fluorophosphate. 300 mg of O-benzoylphenylalanyl-N-benzoylserine was brought into reaction with 420 mg of the ethyl ester of glycine hydrochloride as described above. To the reaction mixture was added 3-5 mg of chymotrypsin which ahd previously been mixed (for 2 hours) with 2 ml of phosphate buffer and a drop of diisopropyl fluorophosphate. The solution remained transparent for 18 hours. Addition of a fresh portion of ferment led to slow precipitation (in the course of 3 hours) of a small quantity of the ethyl ester of L-benzoylphenylalanylglycine, Yield 15 mg. M.p. 146-147°.

2. Reaction of O-benzoyl-D,L-phenylalanyl-N-benzoylserine with the ethyl ester of D,L-phenylalanine. 1 g of the ethyl ester of phenylalanine hydrochloride was dissolved in the equivalent quantity of 1 N alkali. The resulting oil was decanted and mixed with a solution of 460 mg of O-benzoylphenylalanyl-N-benzoylserine in the minimum quantity of alcohol and the equivalent quantity of 1 N alkali. Addition was then made of the mother liquor remaining after separation of the ester of phenylalanine. This was followed by a phosphate buffer and (at pH 7.8) , chymotrypsin (2-3 mg). Particles of the ferment began to intermingle nearly instantaneously with the precipitate which consisted of the ethyl ester of benzoyl-L-phenylalanylphenylalanine. After an hour the reaction mixture was diluted with water and the precipitate was filtered off. The yield of ethyl ester of benzoyl-L-phenylalanylphenylalanine was 90 mg (46% calculated on the O-benzoyl-L-phenylalanyl-N-benzoylserine). M.p. (after numerous recrystallizations from aqueous alcohol) 146-148°, $[\alpha]_D^{18}$ − 36.5 ± 1.2° (0.1204 g in 315 ml of alcohol).

Found %: C 73.09, 73.16; H 6.36, 6.56. $C_{27}H_{28}O_4N_2$. Calculated %: C 72.98; H 6.31.

The mother liquor remaining after separation of the ester of the benzoyl dipeptide was acidified. The precipitate was found to be optically active with $[\alpha]_D^{18}$ + 11.3 ± 0.9° (0.2703 g in 35 ml of anhydrous alcohol). A blank experiment without ferment was run under similar conditions. No outward change was observed after an hour. Addition of chymotrypsin to the solution caused immediate precipitation of a substance identical with that isolated from the main experiment with the ethyl ester of benzoyl-L-phenylalanylphenylalanine.

In another blahk experiment, ferment was not added to the reaction mixture but the solution was acidified In this case, out of 100 mg of O-benzoylphenylalanyl-N-benzoyl serine taken for the experiment, 73 mg was recovered.

3. Reaction of O-benzoyl D'L-phenylalanyl-N-benzoylserine with the ethyl ester of D,L-leucylglycine. To a solution of 460 mg of O-benzoylphenylalanyl-N-benzoylserine in the minimum quantity of alcohol and the equivalent quantity of 1 N alkali was added a solution of 1.26 g of the hydrochloride of the ethyl ester of leucylglycine in the equivalent quantity of 1 N alkali, 2 ml of phosphate buffer and (at a pH of 7.8) 2-3 mg of chymotrypsin. A precipitate at once started to come down. It was filtered off on the following day and recrystallized from aqueous alcohol. Yield of ethyl ester of benzoyl-L-phenylalanylleucylglycine 150 mg (68%); m.p. 198.5-199°; $[\alpha]_D^{20}$ -46.3 ± 3.0° (32.8 mg in 2 ml of alcohol).

Found %: C 66.68, 66.57; H 7.31, 7.37; N 9.07, 9.25. $C_{26}H_{33}O_5N_3$. Calculated %: C 66.81; H 7.06; N 8.99.

In a similar blank experiment, a minute quantity of the ethyl ester of benzoylphenylalanine with m.p. 94-95° came down after 3 days.

4. Reaction of O-benzoyl-D,L-phenylalanyl-N-benzoylserine with the ethyl ester of glycylglycine. To a solution of 460 mg of O-benzoylphenylalanyl-N-benzoylserine in the minimum quantity of alcohol and the equivalent quantity of 1 N alkali was added a solution of 1.0 g of the hydrochloride of the ethyl ester of glycylglycine in the equivalent quantity of alkali, 2 ml of phosphate buffer and (at pH 7.82) 2-3 mg of chymotrypsin. An emulsion immediately started to form around the particles of ferment and slowly settled down in the form of an oil. After half an hour, the oil was collected, washed with alkali, acid and water, and dried. The oil solidified after standing for a long time; weight 50 mg. A few milligrams of the ethyl ester of benzoylphenylalanylglycylglycine were obtained after numerous recrystallizations from aqueous alcohol; m.p. 151-152°. The compound gives an intense tripeptide biuret reaction and a negative ninhydrin reaction and does not contain free carboxyl. After hydrolysis, glycine and phenylalanine were detected on the chromatogram in phenol-water as solvents. Hydrolysis was effected with 20% HCl at 115° for 4 hours.

5. Reaction of O-hippuryl-N-benzoylserine with the ethyl ester of glycine. To a solution of 350 mg of O-hippuryl-N-benzoylserine in 2 ml of alcohol, neutralized with 1 N alkali, was added a solution of 750 mg of the ethyl ester of glycine hydrochloride in the equivalent quantity of 1 N alkali, 2 ml of phosphate buffer and (at pH 8) 2-3 mg of chymotrypsin. After 2 days, the transparent solution was evaporated to a small volume and the precipitate was filtered off and recrystallized from water. Yield of ethyl ester of benzoylglycylglycine 20 mg (15%); m.p. 113-115°.

A blank experiment was run under similar conditions. On evaporation of the solution the salt of O-hippuryl-N-benzoylserine with the ethyl ester of glycine was isolated. M.p. 151-153° (decomp.). The salt gave a positive reaction with ninhydrin.

6. Hydrolysis of N-benzoyl-O-peptides of serine by chymotrypsin. A weighed quantity of N-benzoyl-O-benzoylphenylalanylserine was dissolved in the minimum quantity of alcohol and the solution was neutralized with 0.1 N NaOH. Addition was then made of 2 ml of phosphate buffer and (at pH 8) of 2-3 mg of chymotrypsin. The pH was kept constant by addition of 0.1 N NaOH. Results of hydrolysis are shown in the diagram.

## SUMMARY

It is shown that O-peptides of N-benzoylserine and of N-benzoylthreonine can serve as carriers of the amino acid residue in the fermentative synthesis of peptides. O-Peptides of N-benzoylserine and N-benzoylthreonine react with esters of amino acids and peptides under the action of chymotrypsin to give new N-peptides. O-Benzoylphenylalanyl-N-benzoylserine reacts with great ease.

## LITERATURE CITED

[1] M. M. Botvinik, S. M. Avaeva, M. I. Konovalova and V. I. Ostoslavskaia, J. Gen. Chem., 27, 1910 (1957).*

[2] M. M. Botvinik and S. M. Avaeva, Proc. Acad. Sci. USSR 112, 1053 (1957).*

[3] H. Neurath and G. W. Schwert, Chem. Revs. 46, 69 (1950).

[4] Brenner, Muller and Pfister, Helv. Chim. Acta 33, 538 (1950); M. Brenner, E. Sailer, and K. Rufenacht, l. c., 34, 2098 (1951).

---

*Original Russian pagination. See C.B. Translation.

[5] H. Tauber, J. Am. Chem. Soc. 74, 847 (1952).

[6] I. L. Kaganova and V. N. Orekhovich, Proc. Acad. Sci. USSR 95, 1259 (1954).

[7] N. N. Lestrovaia and S. R. Mardashev, Problems of Medical Chemistry 2, 294 (1956).

[8] M. M. Botvinik S. M. Avaeva and E. A. Mistriukov, Proc. Acad. Sci. USSR 82, 727 (1952); J. Gen. Chem. 24, 2084 (1954);* P. Desnuelle and A. Casal, Biochim., biophys. Acta 2, 64 (1948); D. F. Elliot, Biochem. J. 50, 542 (1952); P. Desnuelle, and G. Bonjour; Biochim,, biophys. Acta 7, 451 (1951); L. K. Ramachandran and W. B. McConnell, Canad. J. Chem. 33, 1638 (1955).

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*Original Russian pagination. See C.B. Translation.

# INVESTIGATION OF THE EXCHANGE REACTION OF OXY RADICALS WITH RADICALS OF ORGANOMAGNESIUM COMPOUNDS

## III. INTERACTION OF ORGANOMAGNESIUM COMPOUNDS WITH MIXED ORGANOSILICON ACETALS

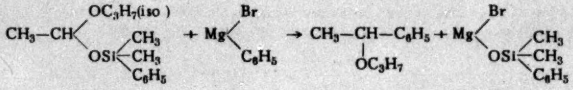
M. F. Shostakovskii, M. R. Kulibekov, and I. A. Shikhiev.

In the preceeding papers [1] we studied the action of a Grignard reagent on mixed and symmetrical organic acetals. It was found that in mixed acetals the heavy oxy radicals are the first to undergo exchange with the radical of the Grignard reagent with formation of the corresponding ethers. Concerning exchange of radicals in symmetrical acetals, we find the following sequence: OAr > OAlk > $OCH_2C_6H_5$. We attribute this pattern of exchange of oxy radicals by Grignard reagent radicals to a certain conjugation effect which causes one of the oxy radicals to become more labile.

It was of interest to investigate the analogous reaction of mixed organosilicon acetals [2] and to clarify the influence of silicon on the mobility of the oxy radicals in acetals. As we know, acetals of the aliphatic series easily undergo symmetrization, while fatty-aromatic acetals are not susceptible to this transformation and break down into vinyl alkyl ethers and phenol when heated. In this respect the mixed organosilicon acetals behave more like the alkyl-aryl acetals, and their symmetrization is accompanied by a series of other reactions. Like the alkyl-aryl acetals [3] they break down [4] when heated. The possibility of existence of mixed organosilicon acetals in two equilibrium forms has been demonstrated [5].

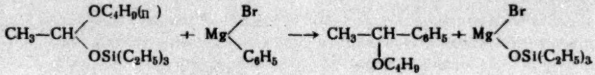
In the present work we studied the interaction of Grignard reagent with mixed organosilicon acetals and arrived at the conclusion that an oxy radical containing a silicon atom is susceptible to exchange regardless of whether the silicon atom is directly attached to oxygen or is in a more distant position. In both bases we obtained the corresponding ethers.

(I)



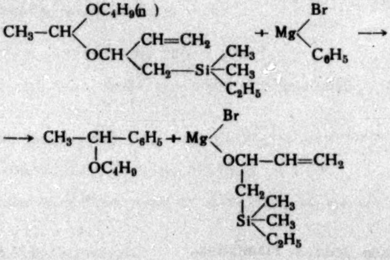
$$CH_3-CH\left\langle{OC_3H_7(iso) \atop OSi(CH_3)_2C_6H_5}\right. + Mg\left\langle{Br \atop C_6H_5}\right. \rightarrow \underset{OC_3H_7}{CH_3-CH-C_6H_5} + Mg\left\langle{Br \atop OSi(CH_3)_2C_6H_5}\right.$$

(II)



$$CH_3-CH\left\langle{OC_4H_9(n) \atop OSi(C_2H_5)_3}\right. + Mg\left\langle{Br \atop C_6H_5}\right. \longrightarrow \underset{OC_4H_9}{CH_3-CH-C_6H_5} + Mg\left\langle{Br \atop OSi(C_2H_5)_3}\right.$$

(III)



$$CH_3-CH\left\langle{OC_4H_9(n) \atop OCH\left\langle{CH=CH_2 \atop CH_2-Si(CH_3)_2C_2H_5}\right.}\right. + Mg\left\langle{Br \atop C_6H_5}\right. \longrightarrow$$

$$\longrightarrow \underset{OC_4H_9}{CH_3-CH-C_6H_5} + Mg\left\langle{Br \atop \underset{CH_2-Si(CH_3)_2C_2H_5}{OCH-CH=CH_2}}\right.$$

The dimethylphenylsilanol and triethylsilanol formed under the reaction conditions dimerize with formation of the corresponding siloxanes. The alcohol (1-dimethylethylsilyl-3-buten-2-ol) obtained during reaction (III) does not dimerize. It should be noted that the oxy radical of isopropyldimethylphenylsilyl acetal (I) more easily enters into the exchange reaction than the oxy radical of butyltriethylsilyl acetal (II), and the latter more easily than the oxy radical of butyl- α-vinyl- β-dimethylethylsilylethyl acetal (III). These differences are evidently associated not only with the proximity of the silicon to the oxygen but with the presence of the phenyl radical.

We convey thanks to co-workers at the Institute of Organic Chemistry of the Academy of Sciences of the USSR, Kh. I. Kondrat'ev and S. I. Sadykh-zade, for kindly placing some of the starting substances at our disposal.

## EXPERIMENTAL

1. Interaction of isopropyldimethylphenylsilyl acetal (I) with phenyl magnesium bromide. Phenyl magnesium bromide was prepared in the usual manner from 3 g of magnesium and 19 g of bromobenzene; the reflux condenser was thereupon replaced by a sloping condenser and the ether was distilled off. At 60° dropwise addition with stirring was commenced of the acetal (I) (11 g) with b.p. 111-111.5 (14 mm), $n_D^{20}$ 1.4737, $d_4^{20}$ 0.9410. The temperature rose sharply and at 90-100° the reaction mixture had changed into a brown suspension. After the whole quantity of acetal had been added, the reaction mixture was stirred for another hour and left overnight. The product was then decomposed with water acidified with acetic acid. The dark-brown oily layer was separated from the aqueous layer and treated with 10% hydrochloric acid (to hydrolyze the unreacted acetal); it was then washed and dried with sodium sulfate. Distillation in vacuo (2 mm) gave 4.6 g (60.68%) of substance with b. p. 68-70°, $d_4^{20}$ 0.9149, $n_D^{20}$ 1.4840; this was the isopropyl ether of phenyl sec. ethyl alcohol [6] Redistillation of the residue gave 3.2 g of bis-dimethylphenylsiloxane [7] with b.p. 112-113.5° (2 mm), $d_4^{20}$ 0.9868 $n_D^{20}$ 1.5177.

2. Reaction of butyltriethylsilyl acetal (II) with phenyl magnesium bromide. Phenyl magnesium bromide was prepared from 4 g of magnesium turnings and 26 g of bromobenzene. Dropwise addition of 20 g of (I) with b.p. 91-92° (10 mm), $n_D^{22}$ 1.4266 to the Grignard reagent was made under the conditions of the preceding experiment. The temperature of the reaction mixture rose to 85° with progressive distillation of the ether. After the acetal had been added, the heated reaction mixture was stirred for another 2 hours. It should be noted that butyltriethylsilyl acetal enters less readily into exchange reaction than the preceding acetal under similar conditions. The product was decomposed with water and worked up as in the preceding experiment. Two distillations in vacuo gave 8.72 g (57.2%) of a substance with b.p. 80-82° (1 mm), $d_4^{20}$ 0.9090, $n_D^{20}$ 1.4822, which was the butyl ether of phenyl sec. ethyl alcohol [8]. From the residue was isolated 3.84 g of hexaethyldisiloxane with b.p. 130-132° (12 mm), $d_4^{20}$ 0.8578, $n_D^{20}$ 1.4329 [9].

3. Reaction of butyl-α-vinyl- β-dimethylethylsilylethyl acetal (III) with phenyl magnesium bromide. The starting (III) was prepared in 78.8% yield from vinyl butyl ether and 1-dimethylethylsilyl-3-buten-2-ol [10].

B.p. 94-94.5° (1 mm), $n_D^{20}$ 1.4360, $d_4^{20}$ 0.8545, $MR_D$ 79.06; calculated 79.65.

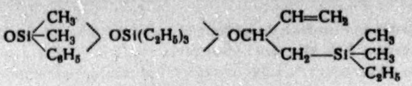
Phenyl magnesium bromide was prepared from 4 g of magnesium and 26 g of bromobenzene. 21 g of the organosilicon acetal was added dropwise at 105°. The reaction mass was heated (120°) with stirring for about 2 hours and left overnight. Appropriate working-up was followed by distillation in vacuo to give 3.45 g of dimethylethylsilyl-3-buten-2-ol [11], b.p. 48-49° (2 mm), $n_D^{20}$ 1.4473, $d_4^{20}$ 0.8555, and 7.7 g (53.14%) of phenyl sec. ethyl alcohol [8] with b.p. 78-80° (2 mm), $d_4^{20}$ 0.9083, $n_D^{20}$ 1.4865. Crystals of diphenyl separated out in the condenser.

## SUMMARY

1. A study was made of exchange reactions of the oxy radicals of mixed organosilicon acetals with radicals of organomagnesium compounds.

2. It was shown that oxy radicals containing a silicon atom enter into exchange reactions.

3. It was established that such radicals exchange with Grignard radicals in the following order of facility:



$$\mathrm{OSi}\begin{matrix}\mathrm{CH_3}\\ \mathrm{CH_3}\\ \mathrm{C_6H_5}\end{matrix} > \mathrm{OSi(C_2H_5)_3} > \mathrm{OCH}\begin{matrix}\mathrm{CH{=}CH_2}\\ \mathrm{CH_2{-}Si}\begin{matrix}\mathrm{CH_3}\\ \mathrm{CH_3}\\ \mathrm{C_2H_5}\end{matrix}\end{matrix}$$

## LITERATURE CITED

[1] M. F. Shostakovskii and M. R. Kulibekov, J. Gen. Chem. 28, 578, 951 (1957).*

[2] M. F. Shostakovskii, I. A. Shikhiev and D. A. Kochkin, Bull. Acad. Sci. USSR, Div. Chem. Sci. 5, 940 (1953).

[3] M. F. Shostakovskii, J. Gen. Chem. 20, 608 (1950);* M. F. Shostakovskii, V. I. Mikhant'ev and N. N. Ovchinnikova, Bull. Acad. Sci. USSR, Div. Chem. Sci. 6, 1099 (1952).*

[4] M. F. Shostakovskii, Kh. I. Kondrat'ev and V. I. Beliaev, Proc. Acad. Sci. USSR 100, 287 (1955).

[5] M. F. Shostakovskii, I. A. Shikhiev and V. I. Beliaev, J. Gen. Chem. 26, 706 (1956). *

[6] A. E. Chichibabin and S. A. Elgazin, J. Russ. Phys. Chem. Soc. 46, 802 (1914).

[7] V. I. Beliaev, Dissertation (Moscow, 1956).

[8] I. P. Tsukervanik and N. G. Simkhaev, J. Gen. Chem. 20, 310 (1950). *

[9] K. A. Andrianov, Organosilicon Compounds [In Russian] (Moscow, 1955), p. 414.

[10] I. A. Shikhiev, M. F. Shostakovskii and N. V. Komarov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1957, 1132.

[11] S. I. Sadykh-zade and A. D. Petrov, Proc. Acad. Sci. USSR, Div. Chem. Sci. 112, No. 4 (1957). *

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*Original Russian pagination. See C.B. Translation.

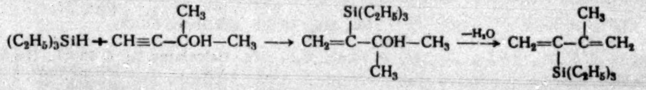
# SYNTHESIS AND TRANSFORMATIONS OF BUTADIENYLSILANES

S. I. Sadykh-zade and A. D. Petrov

Butadienylsilanes or trialkylsilylbutadienes, like homologs of butadiene, can be synthesized with substituents located at the first or second carbon of the butadiene chain. The first representative of the trialkylsilylbutadiene series was prepared [1] by selective hydrogenation of trialkylsilylvinylacetylene.

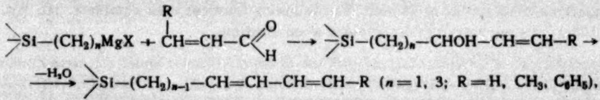
$$R_3Si-C\equiv C-CH=CH_2 + H_2 \longrightarrow R_3Si-CH=CH-CH=CH_2$$

2-Trialkylsilylbutadiene was obtained [2] by the reaction scheme:



$$(C_2H_5)_3SiH + CH\equiv C-\overset{CH_3}{\overset{|}{C}}OH-CH_3 \longrightarrow CH_2=\overset{Si(C_2H_5)_3}{\overset{|}{C}}-\underset{\underset{CH_3}{|}}{C}OH-CH_3 \xrightarrow{-H_2O} CH_2=C-\overset{CH_3}{\overset{|}{\underset{\underset{Si(C_2H_5)_3}{|}}{C}}}=CH_2$$

In the present investigation, a short communication on which was recently published [3], we studied the synthesis of 1-trialkylsilylbutadienes according to the reaction steps:



$$>Si-(CH_2)_nMgX + \overset{R}{\overset{|}{C}}H=CH-C\overset{O}{\underset{H}{<}} \longrightarrow >Si-(CH_2)_n-CHOH-CH=CH-R \rightarrow$$
$$\xrightarrow{-H_2O} >Si-(CH_2)_{n-1}-CH=CH-CH=CH-R\ (n=1,\ 3;\ R=H,\ CH_3,\ C_6H_5),$$

i.e., by dehydration of unsaturated organosilicon alcohols with an alcoholic group ether in the β- or δ-position. The method is interesting because it offers the possibility of synthesizing butadienylsilanes in which the silicon atom is at various distances from the butadiene chain. Judging by the data of Table 1, the yield of alcohols is little influenced by the character of the Grignard reagent or by the character of the radicals attached to the silicon atom. On the other hand, the yield of butadienylsilanes varied over extremely wide limits (Table 2). It was lower in the case of β-alcohols, and it fell by a factor of 2 to 2.5 in this series with progressive substitution of the methyl radical by ethyl, due to the secondary reaction of β-breakdown. It is interesting to note that in respect of β-breakdown these alcohols can be classed in two groups:

$$>Si-CH_2-CHOH-CH=CH_2 \text{ and } >Si-CH_2-CHOH-CH=CH-R.$$

Alcohols of the first group are dehydrated with little β-breakdown; alcohols of the second group with R = $CH_3$ are dehydrated with nearly quantitative β-breakdown; when R = $C_6H_5$, dehydration occurred even on simple distillation, as in the case of the saturated β-alcohol $>Si-CH_2-CHOH-CH_3$ studied by Whitmore [4]. This difference is accounted for by the influence of the substituent R on the direction of shift of the electrons. The effect is to increase the polarization and thereby to weaken the Si-C bond. This shift takes effect only along the system of conjugated bonds resulting from dehydration of the β-alcohols, and has no influence on the Si-C bond in the case of δ-alcohols, i.e. when the silicon atom is separated from the conjugated grouping by two carbons linked by a single bond. Thus, trialkyl-β-methylbutadienylethylsilane is found in 78% yield.

$$>Si-CH_2-CH_2-CH_2-CHOH-CH=CH-CH_3 \xrightarrow{-H_2O}$$

$$>Si-(CH_2)_2-CH=CH-CH=CH-CH_3$$

A study was made of the behavior of butadienylsilanes obtained by dehydration of β-alcohols in condensations with maleic anhydride, acrolein and acrylonitrile under the usual conditions of the Diels-Alder reaction. In all cases the reaction went with high yields of the corresponding products of synthesis. The cyclic aldehydes gave hydrazones with 2,4-dinitrophenylhydrazine. Hydrolysis of the maleic anhydride adduct gave a dibasic acid.

Dehydration of the β-alcohols gave the dimers in addition to the monomeric butadienylsilanes. The properties of these dimers, which are arbitrarily formulated as $[R_3Si-CH=CH-CH=CH_2]_2$, are presented in Table 2 (compound XVII-XIX). It should be noted that these properties did not alter when the dimers were boiled for several hours; they are apparently silicon-containing alkenylcyclohexenes (structural analogs of vinylcyclohexene), formed by cyclodimerization of butadiene. Boiling converts the monomeric butadienylsilanes both into dimers and higher molecular rubber-like polymers. Dehydration of δ-alcohols gives predominantly monomeric silicodiolefins in high yields; dimers are scarcely formed here – probably due to greater steric hindrance.

## EXPERIMENTAL

We shall not describe the synthesis of the starting Grignard reagents* since it has already been described [5]. We give only the properties of methyldiethyl-γ-bromopropylsilane, which was prepared for the first time.**

B.p. 218° at 750 mm, $n_D^{20}$ 1.4680, $d_4^{20}$ 1.1039, $MR_D$ 56.26; calculated 56.48.

Found %: C 43.35; H 8.56; Si 12.21; Br 34.41. $C_8H_{19}SiBr$. Calculated %: C 43.07; H 8.52; Si 21.56; Br 35.85.

1-Trimethylsilyl-3-buten-2-ol (I). 170 g of trimethyl-α-chloromethylsilane was added dropwise with cooling to 52.8g Mg in 700 ml of ether. To the Grignard reagent (cooled with ice) was added 123.2 g of freshly distilled acrolein with b.p. 51-52°. The reaction was violent and heat was released. After distillation of the ether, the product was fractionated at 24 mm. The following fractions were obtained: 1st, b.p. 35-70°, 20 g; 2nd, 70-75°, 160 g ; the residue (40 g) decomposed when distilled.

Other secondary alcohols were obtained with use of crotonaldehyde under the same conditions as above: 1-dimethylethylsilyl-2-ol (II), 1-methyldiethylsilyl-3-buten-2-ol (III), 1-dimethylbutylsilyl-3-buten-2-ol (IV), 1-triethylsilyl-3-buten-2-ol (V), 1-dimethylethylsilyl-3-penten-2-ol (VI), 1-trimethylsilyl-5-hexen-4-ol (VII), 1-methyldiethylsilyl-5-hexen-4-ol (VIII), and 1-methyldiethylsilyl-5-hepten-4-ol (IX) (properties and yields are given in Table 1).

We shall consider in more detail the products of synthesis of 1-methyldiethylsilyl-5-hexen-4-ol (VIII), obtained by us in quantity of 180 g. They were fractionated at 2 mm to give: 1st fraction, 30-94°, 20 g; 2nd fraction, 94-97°, 110 g; 3rd fraction, 97-150°, 21 g; the residue of 17 g did not distill without decomposition. Redistillation in a column gave, apart from the secondary alcohol, by-products of the reaction. Methyldiethylpropylsilane, for example, was isolated from the 1st fraction:

B.p. 143.5°, $n_D^{20}$ 1.4252, $d_4^{20}$ 0.7619, $MR_D$ 48.45; calculated 48.80.

Found %: C 66.64; H 13.90; Si 19.10. $C_8H_{20}Si$. Calculated %: C 66.70; H 13.90; Si 19.44.

The 3rd fraction yielded a substance with b.p. 127.5-129° at 2 mm, identified as 1,6-bis-methyldiethylsilylhexane:***

$n_D^{20}$ 1.4568, $d_4^{20}$ 0.8502, $MR_D$ 91.77; calculated 92.09.

Found %: C 66.80; H 13.04. $C_{16}H_{38}Si$. Calculated %: C 67.13; H 13.3.

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* I. Avgushevich [3] participated in the synthesis of α-chloromethyltrialkylsilanes.

** $(CH_3)(C_2H_5)SiCH_2CH_2CH_2Br$.

*** $(CH_3)(C_2H_5)Si(CH_2)_6Si(C_2H_5)_2(CH_3)$.

TABLE 1

| Compound No. | Compound | Boiling point (pressure in mm) | | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ | | Yield (в %) | Found (%) | | | | Empirical formula | Calculated (%) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | found | calc. | | C | H | OH | Si | | C | H | OH | Si |
| I | $(CH_3)_3Si-CH_2-CHOH-CH=CH_2$<br>1-Trimethylsilyl-3-buten-2-ol | 70—70.5 | (24) | 1.4427 | 0.8427 | 45.06 | 45.25 | 50.5 | 57.45,<br>57.25 | 11.10,<br>11.05 | 1.1,<br>0.87 | 19.15,<br>18.84 | $C_7H_{16}OSi$ | 58.27 | 11.17 | 1.0 | 19.45 |
| II | $(CH_3)_2(C_2H_5)Si-CH_2-CHOH-CH=CH_2$<br>1-Dimethylethylsilyl-3-buten-2-ol | 74—75 | (9) | 1.4492 | 0.8528 | 49.81 | 49.88 | 68.7 | 60.20,<br>60.09 | 11.42,<br>11.41 | 0.96,<br>1.04 | 17.65,<br>17.69 | $C_8H_{18}OSi$ | 60.70 | 11.46 | 1.0 | 17.72 |
| III | $(CH_3)(C_2H_5)_2Si-CH_2-CHOH-CH=CH_2$<br>1-Methyldiethylsilyl-3-buten-2-ol | 79—80 | (6) | 1.4611 | 0.8651 | 54.57 | 54.51 | 51.5 | 62.24,<br>62.16 | 11.48,<br>31.68 | 0.888,<br>1.050 | 16.53,<br>16.48 | $C_9H_{20}OSi$ | 62.72 | 11.69 | 1.0 | 16.28 |
| IV | $(CH_3)_2(C_4H_9)Si-CH_2-CHOH-CH=CH_2$<br>1-Dimethylbutylsilyl-3-buten-2-ol | 75—76 | (2.5) | 1.4548 | 0.8501 | 59.40 | 59.14 | 64.7 | | — | 0.915,<br>1.15 | 15.76,<br>15.32 | $C_9H_{20}OSi$ | | — | 1.0 | 15.10 |
| V | $(C_2H_5)_3Si-CH_2-CHOH-CH=CH_2$<br>1-Triethylsilyl-3-buten-2-ol | 76—77 | (2) | 1.4648 | 0.8816 | 58.41 | 59.14 | 53.6 | — | — | 0.927 | — | $C_{10}H_{22}OSi$ | — | — | 1.0 | — |
| VI | $(CH_3)_2(C_2H_5)Si-CH_2-CHOH-CH=CHCH_3$<br>1-Dimethylethylsilyl-3-penten-2-ol | 70—71 | (3) | 1.4583 | 0.8566 | 54.51 | 54.91 | 54.4 | — | — | 1.19,<br>0.958 | — | $C_9H_{20}OSi$ | — | — | 1.0 | — |
| VII | $(CH_3)_3Si-(CH_2)_3-CHOH-CH=CH_2$<br>1-Trimethylsilyl-5-hexen-4-ol | 70—71 | (3) | 1.4422 | 0.8352 | 54.62 | 54.51 | 80.0 | 62.32,<br>62.30 | 12.20,<br>12.30 | — | 17.17 | $C_{11}H_{24}OSi$ | 62.66 | 11.80 | — | 16.37 |
| VIII | $(CH_3)(C_2H_5)_2Si-(CH_2)_3-CHOH-CH=CH_2$<br>1-Methyldiethylsilyl-5-hexen-4-ol | 87—87.5 | (1) | 1.4570 | 0.8648 | 63.11 | 63.77 | 64.0 | — | — | — | 14.56 | $C_{11}H_{24}OSi$ | — | — | — | 14.02 |
| IX | $(CH_3)(C_2H_5)_2Si-(CH_2)_3-CHOH-CH=CH-CH_3$<br>1-Methyldiethylsilyl-5-hepten-4-ol | 102.0 | (1) | 1.4605 | 0.8653 | 67.93 | 68.40 | 70.0 | 67.40,<br>67.60 | 12.40,<br>12.23 | — | 12.66,<br>12.82 | $C_{12}H_{26}OSi$ | 67.22 | 12.22 | — | 13.10 |

Consequently, the halide, in which the silicon is in the γ-position to the halogen and no longer exerts an influence on the latter, reacts with aldehydes in a similar manner to silicon-free RMgX to form by-products R-R and R-H (compare [6]) in addition to the main product – the secondary alcohol. Allyl alcohol was presumably also formed here and came over with the ether.

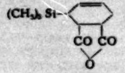
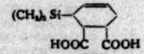
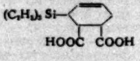
1-Trimethylsilylbutadiene (X). 0.5 g of $KHSO_4$ was added every 15 minutes to 144 g of 1-trimethylsilyl-3-buten-2-ol (I) in a flask fitted with a column. After 2-hours' heating on a water bath, the operation was completed. After separation of the water, the product of dehydration was washed with 3% $Na_2CO_3$ and dried with $Na_2SO_4$. It was fractionated in a column at atmospheric pressure with addition of hydroquinone. The following fractions were obtained: 1st, to 98.5°, 4 g; 2nd, 98.5-99°, 25 g; 3rd, 99-113.5°, 4 g; 4th, 113.5°, 50 g; residue 13 g. The product of β-decomposition $(CH_3)_3SiOSi(CH_3)_3$ was identified in the 2nd fraction. The 4th fraction contained 1-trimethylsilylbutadiene (X). Redistillation of the residue at 3 mm gave a dimer with b.p. 95°. The residue from the redistillation was a soluble and fusible polymer. Under similar conditions we prepared 1-dimethylethylsilylbutadiene (XI), 1-methyldiethylsilylbutadiene (XII), and 1-triethylsilylbutadiene (XIII). Yield and analytical results are presented in Table 2.

1-Trimethylsilyl-3,5-hexadiene (XIV). 50 g of 1-trimethylsilyl-5-hexen-4-ol (VII) and a few drops of concentrated $H_2SO_4$ were put into a flask fitted with a reflux condenser. The mixture was heated for 1 hour at 100-115°. The water was separated, and the product was dried and fractionated to give the diolefinic silicohydrocarbon b.p. 162-162.5°, weight 34 g. The same conditions were employed in the preparation of 1-methyldiethylsilyl-3,5-hexadiene (XV) and 1-methyldiethylsilyl-3,5-heptadiene (XVI)(see Table 2 for properties and analytical data).

Adduct with maleic anhydride (XX). 2 g of maleic anhydride and 1.5 g of trimethylbutadienylsilane were heated for 30 minutes at 100-115°. After cooling, the mixture was poured into a beaker of water. The crystals were washed with water and recrystallized from acetone and ligroine. M.p. 116°. The adduct with triethylbutadienylsilane had m.p. 124.5°. Boiling with water converted the adducts into dibasic acids (Table 2, compounds XXI and XXII).

1-Trimethylsilyl-5-nitrilo-2-cyclohexene. A 100-ml ampoule containing 12.6 g of trimethyl-

TABLE 2

| Compound No. | Compound | B. p. (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ found | $MR_D$ calc. | Выход (в %) | Found (%) C | Found (%) H | Found (%) Si | Empirical formula | Calculated (%) C | Calculated (%) H | Calculated (%) Si |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (X) | $(CH_3)_3Si-CH=CH-CH=CH_2$<br>1-Trimethylsilylbutadiene | 113.5° (759) | 1.4480 | 0.7538 | 44.84 | 43.23 | 40 | 65.54,<br>65.44 | 11.34<br>11.59 | 22.38<br>22.13 | $C_7H_{14}Si$ | 66.51 | 11.11 | 22.19 |
| (XI) | $(CH_3)_2(C_2H_5)Si-CH=CH-CH=CH_2$<br>1-Dimethylethylsilylbutadiene | 138—138.5 (751) | 1.4490 | 0.7695 | 48.89 | 47.86 | 35 | 67.97<br>68.15 | 11.72<br>11.86 | 19.61<br>19.68 | $C_8H_{16}Si$ | 68.51 | 11.49 | 20.0 |
| (XII) | $(CH_3)(C_2H_5)_2Si-CH=CH-CH=CH_2$<br>1-Methyldiethylsilylbutadiene | 162—162.5 (752) | 1.4585 | 0.7876 | 53.5 | 52.49 | 17.3 | 69.25<br>69.28 | 12.00<br>11.90 | 17.78<br>18.03 | $C_9H_{18}Si$ | 70.05 | 11.69 | 18.18 |
| (XIII) | $(C_2H_5)_3Si-CH=CH-CH=CH_2$<br>1-Triethylsilylbutadiene | 184.5—185 (755) | 1.4695 | 0.8070 | 58.15 | 57.12 | 15.0 | 71.30<br>71.00 | 12.50<br>12.45 | 16.10<br>16.23 | $C_{10}H_{20}Si$ | 71.34 | 11.98 | 16.68 |
| (XIV) | $(CH_3)_3Si-CH_2-CH_2-CH=CH-CH=CH_2$<br>1-Trimethylsilyl-3,5-hexadiene | 162.5 (749) | 1.4515 | 0.7777 | 53.47 | 52.49 | 18.0 | 69.50<br>69.40 | 12.50<br>12.62 | 18.36<br>18.35 | $C_9H_{18}Si$ | 70.05 | 11.69 | 18.18 |
| (XV) | $(CH_3)(C_2H_5)_2Si-CH_2-CH_2-CH=CH-CH=CH_2$<br>1-Methyldiethylsilyl-3,5-hexadiene | 78—79 (5.5) | 1.4648 | 0.8130 | 62.08 | 61.75 | 30 * | — | — | 15.10<br>15.19 | $C_{11}H_{22}Si$ | — | — | 15.37 |
| (XVI) | $(CH_3)(C_2H_5)_2Si-CH_2-CH_2-CH=CH-CH=CH-CH_3$<br>1-Methyldiethylsilyl-3,5-heptadiene | 75—75.5 (1) | 1.4740 | 0.8127 | 67.92 | 66.38 | 79 | 73.30<br>73.45 | 12.57<br>12.60 | 13.50<br>13.48 | $C_{12}H_{24}Si$ | 73.36 | 12.32 | 14.27 |
| (XVII) | $[(CH_3)_3Si-CH=CH-CH=CH_2]_2$ | 95 (3.5) | 1.4790 | 0.8640 | 82.84 | 83.14 | 2.5 | 65.71<br>65.87 | 11.19<br>11.07 | 21.74<br>21.46 | $C_{14}H_{28}Si_2$ | 66.51 | 11.11 | 22.19 |
| (XVIII) | $[(CH_3)_2(C_2H_5)Si-CH=CH-CH=CH_2]_2$ | 117—118 (2.5) | 1.4830 | 0.8635 | 92.72 | 92.40 | 10 | 67.67<br>67.77 | 11.41<br>11.42 | 19.67<br>19.73 | $C_{16}H_{32}Si_2$ | 68.51 | 11.49 | 20.00 |
| (XIX) | $[(CH_3)(C_2H_5)_2Si-CH=CH-CH=CH_2]_2$ | 139—141 (3) | 1.4930 | 0.8849 | 101.65 | 101.65 | 16 | 69.33<br>70.19 | 12.04<br>12.09 | 17.36<br>17.38 | $C_{18}H_{36}Si_2$ | 70.05 | 11.69 | 18.18 |
| (XX) |  | 124.5 ** | — | — | — | — | — | 59.00<br>58.77 | 7.00<br>7.24 | 12.31<br>12.26 | $C_{11}H_{16}O_3Si$ | 58.93 | 7.14 | 12.50 |
| (XXI) |  | 103.0 ** | — | — | — | — | — | — | — | 11.51<br>11.21 | $C_{11}H_{18}O_4Si$ | — | — | 11.57 |
| (XXII) |  | 131–132 ** | — | — | — | — | — | 59.42<br>59.50 | 8.77<br>8.67 | 8.99<br>9.56 | $C_{14}H_{24}O_4Si$ | 59.12 | 8.50 | 9.87 |

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* Part of the product polymerized.

** Melting point.

silylbutadiene, 8 g of acrolein and a crystal of iodine was sealed and heated to 190-210° for 3 hours. Distillation at 2 mm gave 12 g of liquid reaction product which was easily mobile and had a pleasant odor. B.p. 78-78.5°, $d_4^{20}$ , 0.9272, $n_D^{20}$ 1.4820.

Found %: C 66.94; H 9.71; Si 15.60. $C_{10}H_{17}NSi$. Calculated %: C 67.07; H 9.47; Si 15.64.

1-Dimethylethylsilyl-5-carbomethoxy-2-cyclohexene. An ampoule containing 14 g of dimethylethylbutadienylsilane and 12.9 g of freshly distilled methyl acrylate was heated under the preceding conditions to give (distillation at 4 mm) 16 g of product with b.p. 83-84°, $n_D^{20}$ 1.4808, $d_4^{20}$ 0.9865.

Found %: Si 12.57. $C_{12}H_{22}O_2Si$. Calculated %: Si 12.39.

1-Methyldiethylsilyl-2-cyclohexen-5-al. An ampoule containing 10 g of methyldiethylbutadienylsilane and 5 g of freshly distilled acrolein was heated at 170-190° for 1 hour. 5 g of product was isolated by distillation at 2 mm; b.p. 102-103°, $n_D^{20}$ 1.4918, $d_4^{20}$ 0.9518.

Found %: C 68.40; H 10.75. $C_{12}H_{22}OSi$. Calculated %: C 68.49; H 10.54.

The 2,4-dinitrophenylhydrazone of this aldehyde had m.p. 121.0°.

Found %: N 14.56. $C_{18}H_{26}O_4N_4Si$. Calculated %: N 14.35.

1-Triethylsilyl-2-cyclohexen-5-al was synthesized under similar conditions: b.p. 114.5-115.5° at 2 mm, $n_D^{20}$ 1.4955, $d_4^{20}$ 0.9560.

Found %: C 69.54; H 10.10. $C_{13}H_{24}OSi$. Calculated %: C 69.55; H 10.79.

## SUMMARY

1. It is shown that unsaturated β- and γ-silicoorganic alcohols can be synthesized by condensation of Grignard reagents from α- and γ-silicohalides with acrolein and crotonaldehyde. It was established that dehydration of the β-derivatives proceeds with partial β-breakdown (the extent of which is governed by the structure of the alcohol), as well as with secondary formation of dimers and monomers. The γ-alcohols are dehydrated without degradation and without formation of dimers.

2. Butadienylsilanes were subjected to Diels-Alder condensation with acrolein, acrylic ester, acrylonitrile and maleic anhydride.

## LITERATURE CITED

[1] A. D. Petrov, S. I. Sadykh-zade and Iu. P. Egorov, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1954, 722. •

[2] A. L. Shchukovskaia and A. D. Petrov, J. Gen. Chem., 26, 3338 (1956).•

[3] S. I. Sadykh-zade, I. Avgushevich and A. D. Petrov, Proc. Acad. Sci. USSR, 112, 662 (1957).•

[4] F. C. Whitmore, L. H. Sommer, J. Gold, and R. E. van Strien, J. Am. Chem. Soc., 69 1551 (1945).

[5] V. A. Ponomarenko and V. F. Mironov, Proc. Acad. Sci. USSR, 94, 485 (1954).

[6] A. D. Petrov, Z. K. Shunina and Iu. A. Ol'dekop, J. Gen. Chem., 14, 498 (1944).

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•Original Russian pagination. See C.B. Translation.

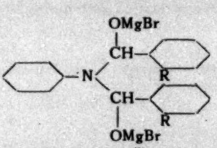
# REACTIONS OF MAGNESYLAMINES

## VI. STERIC HINDRANCE IN THE ARAMIDATION OF AROMATIC ALDEHYDES WITH THE HELP OF N,N'-bis-(HALOMAGNESIUM)ARYLAMINES

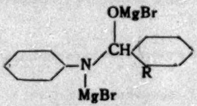
P. A. Petinunin and L. A. Tetiueva

In order to clarify the influence of steric hindrance during amidation of aromatic aldehydes with the help of dimagnesylamines, we ran a series of experiments with aldehydes and amines containing various substituents in the ortho-position. The experiments showed that aldehydes and dimagnesylamines exert steric hindrance to different degrees. Aldehydes are characterized by greater steric hindrance. Introduction of one substituent in the ortho-position, for example, blocks the aldehyde group to such a extent that the aramidation of such aldehydes becomes substantially impossible. This was demonstrated in the reaction between o-toluidine and o-methoxybenzaldehyde on the one hand and N,N'-bis-(bromomagnesium)aniline on the other. Experiments were performed in pyridine solution with a heating period of one hour. Heat was developed when the reactants were stirred, but the original substances were recovered unchanged after decomposition of the reaction mass with dilute hydrochloric acid.

On the basis of our proposed reaction mechanism [1], disproportionation can proceed only in the complex (I), which is formed by reaction of two molecules of aldehyde with one molecule of magnesylamine



(I)

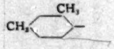
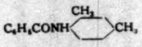
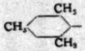
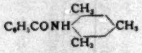
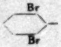
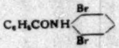
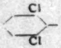
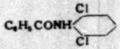


(II)

R=$CH_3$, $CH_3O$.

Disproportionation of the above aldehydes does not occur, and consequently the complex (I) is not formed, the process stopping with formation of complex (II). Complex (I) might have been formed by interaction of (II) with a fresh molecule of aldehyde. This is prevented, however, by steric hindrances which are simultaneously exerted both by (II) and by the aldehyde due to the substituent in the ortho-position.

Steric hindrance by N,N'-bis-(bromomagnesium)arylamines was established by experiments between dimagnesylamines containing substituents in the ortho-position and aldehydes without substituents in that position. Experiments were carried out in a medium of ether or pyridine. Results are presented in the table. We see from the results that the reaction is not appreciably inhibited by dimagnesylamines containing one substituent (Br, Cl, $CH_3$, $OCH_3$) in the ortho-position (experiments 1-6). The yields of the corresponding arylamides are approximately the same as in the case of dimagnesylamines without substituents in the ortho-position, namely: 14-19% in the ether medium and 45-75% in the pyridine medium. These results demonstrate that the presence of one substituent in the ortho-position to the $(BrMg)_2N$ group does not hinder formation of the complex (III), and disproportionation to this complex proceeds normally. A different picture is obtained when experiments are run with dimagnesylamines in which both of the ortho-positions to the $(BrMg)_2N$ group are occupied by sub-

| Expt. No. | Aldehyde | Nature of Ar in $ArN(MgBr)_2$ | Product of reaction * | Yield (in %) | Melting point |  |
|---|---|---|---|---|---|---|
|  |  |  |  |  | our data | literature [2] |
| 1 | $C_6H_5CHO$ | $o$-$BrC_6H_4$— | $C_6H_5CONHC_6H_4Br$-$o$ | 15.6 | 105—107° | 116° |
| 2 |  | $o$-$ClC_6H_4$— | $C_6H_5CONHC_6H_4Cl$-$o$ | 18.9 | 100—101 | 99—101 |
| 3 |  | $o$-$CH_3C_6H_4$— | $C_6H_5CONHC_6H_4CH_3$-$o$ | 14.3 | 142—143.5 | 143 |
| 4 |  |  |  | 44.5 | 192 | 192 |
| 5 | $p$-$BrC_6H_4CHO$ | $o$-$CH_3C_6H_4$— | $p$-$BrC_6H_4CONHC_6H_4CH_3$-$o$ (IV) | 74.58 | 158—159 | — |
| 6 | $p$-$BrC_6H_4CHO$ | $o$-$CH_3OC_6H_4$— | $p$-$BrC_6H_4CONHC_6H_4OCH_3$-$o$ (V) | 70.68 | 136—137.5 | — |
| 7 | $C_6H_5CHO$ |  |  | 13.4 | 204 | 204 |
| 8 |  |  |  (VI) | 0.56 | 177—178 | — |
| 9 |  |  |  (VII) | 0.75 | 158—159 | — |

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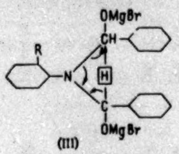
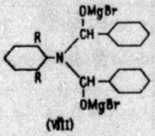
* Ether was the solvent in experiments 1-3, 8 and 9, and pyridine in experiments 4-7.

stituents (experiments 7-9). No heat is developed when benzaldehyde is added to ether solutions of dimagnesylamines prepared from 2,6-dichloro- and 2,6-dibromoanilines. The yields of the corresponding arylamides were negligible. Slightly better results were obtained in a medium of pyridine. The mesidide of benzoic acid, for example, was obtained in a yield of 13.4% (experiment 7). But even this yield is more than 3 times smaller than that for dimagnesylamines without substituents in the ortho-position. Just as in the case of aldehydes, the steric hindrance manifested by dimagnesylamines with substituents in both of the ortho-positions hinders formation of the complex (VIII) in which an oxidation-reduction must take place. Here again the reaction is evidently limited in the main by the equimolar reaction of the starting substances.



(III)

R = Br, Cl, CH$_3$, CH$_3$O.



(VIII)

R = Cl, Br, CH$_3$.

## EXPERIMENTAL

The procedures were the same as those described in the preceding communications. In one experiment 0.0125 mole of N,N'-bis-(bromomagnesium)arylamine was reacted with 0.025 mole of aromatic aldehyde. Arylamides (VI) and (VII) were identified in mixed melting point tests with substances obtained by reaction of ethyl benzoate with dimagnesylamines from 2,6-dibromo- and 2,6-dichloroanilines.

o-Toluidide of p-bromobenzoic acid (IV). Sparingly soluble in ether, more easily soluble in alcohol, toluene, chloroform and acetone. Crystallizes from glacial acetic acid in the form of colorless plates.

The melting points of this compound and of the other newly prepared substances are listed in the table.

Found %: N 4.99, 4.67. C$_{14}$H$_{12}$ONBr. Calculated %: N 4.83.

o-Anisidide of p-bromobenzoic acid (V). Sparingly soluble in ether, and readily soluble in alcohol, acetic acid, benzene and chloroform. Crystallizes from glacial acetic acid in the form of colorless rodlets.

Found %: N 4.42, 4.50. C$_{14}$H$_{12}$O$_2$NBr. Calculated %: N 4.57.

2,6-Dibromoanilide of benzoic acid (VI). Sparingly soluble in ether, readily soluble in acetic acid, alcohol, benzene and acetone. Prisms (from alcohol). Obtained in 75.8% yield by reaction of ethyl benzoate with N,N'-bis-(bromomagnesium)-2-6-dibromoaniline in 1 : 1 ratio. No depression of melting point in a mixed test.

Found %: N 3.84, 3.95. C$_{13}$H$_9$ONBr$_2$. Calculated %: N 3.94.

2,6-Dichloroanilide of benzoic acid (VII). Sparingly soluble in ether, readily soluble in acetic acid, benzene, alcohol and acetone. Prisms (from alcohol). Prepared in 75.2% yield by reaction of equimolar amounts of ethyl benzoate and N,N'-bis-(bromomagnesium)-2,6-dichloroaniline. No depression of melting poin in a mixed test.

Found %: N 5.15, 5.19. C$_{13}$H$_9$ONCl$_2$. Calculated %: N 5.26.

## SUMMARY

1. A study was made of steric hindrance in the aramidation of aromatic aldehydes with the help of N,N'-bis-(halomagnesium)arylamines.

2. It was established that the strongest steric hindrance is exerted by the aldehyde: one substituent in the ortho-position to the aldehyde group substantially rules out the possibility of aramidation.

3. N,N'-bis-(halomagnesium)arylamines exert steric hindrance when both of the ortho-positions relative to the (BrMg)$_2$N group are occupied by substituents.

4. A previously undescribed series of arylamides was prepared and their properties were studied.

## LITERATURE CITED

[1] P. A. Petiunin and L. A. Tetiueva, J. Gen. Chem., 28, 1105 (1958).*

[2] Beilst., XII.

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Perm Pharmaceutical Institute

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*Original Russian pagination. See C.B. Translation.

# SYNTHESIS OF ORGANOPHOSPHORUS COMPOUNDS FROM HYDROCARBONS AND THEIR DERIVATIVES

## VII. OXIDATIVE CHLOROPHOSPHONATION BY MEANS OF ALKYL AND DIALKYLAMIDOPHOSPHORODICHLORIDITES *

Iu. M. Zinov'ev, V. N. Kulakova and L. Z. Soborovskii

Oxidative chlorophosphonation of hydrocarbons and their derivatives had been accomplished previously by means of phosphorus trichloride, alkyldichlorophosphines and aryldichlorophosphines [1]. It has been shown in the present work that one may use alkyl phosphorodichloridites (alkyl dichlorophosphites) and dialkylamidophosphorodichloridites (dialkylaminodichlorophosphines), i.e. compounds in which the hydrocarbon residue is bound to the phosphorus atom through a third element: $RH + 2\,R'XPCl_2 + O_2 \rightarrow RP(O)(XR')Cl + R'XP(O)Cl_2 + HCl$, where R and R' are hydrocarbon radicals and X is oxygen or nitrogen, as the phosphonating agent. We performed the oxidative chlorophosphonation of cyclohexane (with ethyl phosphorodichloridite) and of vinyl chloride (with methyl phosphorodichloridite and dimethylamidophosphordichloridite) with these reagents. As the result of these reactions there were isolated the corresponding phosphonic chlorides which contain the phosphorus-carbon bond.

Oxidative chlorophosphonation of cyclohexane with ethyl phosphorodichloridite led to formation of a mixture of compounds, the separation of which by fractionation turned out to be difficult. Therefore, in order to prove the course of the reaction in accord with the scheme shown above, i.e. to prove the formation of a carbon-phosphorus bond, we treated the resulting mass with water and, from the hydrolysis products, we isolated a substance shown to be cyclohexanephosphonic acid (cyclohexylphosphonic acid).

Oxidative chlorophosphonation of compounds of the ethylene series by alkyl phosphorodichloridites proceeds completely analogously to the reaction which is performed with phosphorus trichloride. This reaction was run with vinyl chloride. Methyl phosphorodichloridite and dimethylamidophosphorodichloridite were used as the phosphonating agents. From the products of the reaction of vinyl chloride and methyl phosphorodichloridite there was isolated a fraction which boiled at 105-115° (5 mm), the main bulk of which consisted of methyl dichloroethylphosphonochloridate. We failed to isolate this compound in the pure state owing to the instability of substances of this type. However, the formation of phosphorus-carbon bond was proved by the preparation from this fraction of the dimethyl ester of dichloroethylphosphonic acid, identical in its properties with a specimen prepared from the previously described chloride of dichloroethylphosphonic acid [2].

$$CH_2{=}CHCl + 2CH_3OPCl_2 + O_2 \longrightarrow C_2H_3Cl_2P(O)(OCH_3)Cl + CH_3OP(O)Cl_2$$
$$C_2H_3Cl_2P(O)(OCH_3)Cl + CH_3OH \longrightarrow C_2H_3Cl_2P(O)(OCH_3)_2 + HCl$$

Oxidative chlorophosphonation of vinyl chloride by dimethylamidophosphorodichloridite proceeds according to the following scheme:

$$CH_2{=}CHCl + 2(CH_3)_2NPCl_2 + O_2 \longrightarrow C_2H_3Cl_2P(O)[N(CH_3)_2]Cl + (CH_3)_2NP(O)Cl_2$$

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* Alkyl and dialkylphosphoramidous dichlorides.

Ethyl ester of N,N-dimethyl-dichloroethylphosphonamidic acid was prepared from the resulting choride of N,N-dimethyl-dichloroethylphosphonamidic acid and sodium ethoxide.

It had been shown previously that oxidative chorophosphonation of vinyl chloride with phosphorus trichloride leads to the formation of two isomeric chlorides of dichloroethylphosphonic acid [2]. The compounds prepared from vinyl chloride in the present work are also evidently isomer mixtures the structures of which may be expressed by the formulas $ClCH_2CHClP(O)(OCH_3)Cl$ and $CHCl_2CH_2P(O)(OCH_3)Cl$ (for products of oxidative chlorophosphonation with methyl phosphorodichloridite) and $ClCH_2CHClP(O)[N(CH_3)_2]Cl$ and $CHCl_2CH_2P(O)[N(CH_3)_2]Cl$ (for the chloride synthesized from dimethylamidophosphorodichloridite). We did not accomplish the isolation of the individual isomers.

## EXPERIMENTAL

1. Oxidative chlorophosphonation of cyclohexane by ethyl phosphorodichloridite. Oxygen was passed through a mixture of 21 g (0.25 mole) of cyclohexane and 180 g. (1.2 moles of ethyl phosphorodichloridite until the reaction ceased. From the reaction mixutre there was isolated 11 g of a fraction which boiled in the interval of 106-112° (3 mm); $d_4^{20}$ 1.2576. The substance passed almost completely into solution on being warmed with thirty ml of water. After the removal of water, crystals were isolated and these were recrystallized from alcohol [m. p. 160-161°]. Cyclohexylphosphonic acid, prepared from the acid chloride synthesized by oxidative chlorophosphonation of cyclohexane by phosphorus trichloride, melted at 162°. The mixed melting point of the two specimens was 161-162°.

Found %: C 44.37, 44.62; H 8.68, 8.71; P 19.47, 19.57. $C_6H_{13}O_3P$. Calculated %: C 43.94; H 8.00; P 18.87.

2. Oxidative chlorophosphonation of vinyl chloride by methyl phosphorodichloridite. a) Oxygen was passed through 200 g of vinyl chloride and 128.2 g (0.96 mole) of methyl phosphorodichloridite at -20° until the reaction ceased. After the removal of low-boiling products, there was distilled 25 g. (12.3%) of a substance boiling at 110-118° (5 mm). The distillation was accompanied by partial decomposition. After a second distillation there was isolated the fraction with b.p. 105-110° (5 mm); $d_4^{20}$ 1.5220; $n_D^{20}$ 1.4693.

Found %: P 14.26, 14.24. $C_3H_6O_2PCl_3$. Calculated %: P 14.65.

b) Eighteen and a half grams of the substance prepared as described above was added dropwise at 10° to 100 ml. of methanol. From the reaction mixture there was isolated 14.5 g. of a substance with b.p. 105-109° (4 mm); $d_4^{20}$ 1.4060; $n_D^{20}$ 1.4508.

c) To 48 g (1.5 moles) of methanol there was added dropwise at -10° 21.6 g (0.1 mole) of dichloroethylphosphonic dichloride.* From the reaction mixture there was isolated a substance boiling at 110-112° (4 mm); $d_4^{20}$ 1.4039; $n_D^{20}$ 1.4510. The yield: 18.1 g (87.5%).

Found %: C 23.26, 23.32; H 4.76, 4.51; P 14.82, 14.34; M 213.5. $C_4H_9OPCl_2$. Calculated %: C 23.20; H 4.38; P 14.96. M 207.01.

3. Oxidative chlorophosphonation of vinyl chloride by dimethylamidophosphorodichloridite: a) Oxygen was passed at -30° through a mixture of 90 g (1.44 moles) of vinyl chloride and 82 g (0.56 mole) of dimethylamidophosphorodichloridite (b.p. 146-148°, $d_4^{20}$ 1.2624; according to data from [3]: b.p. 40° at 10 mm. $d_4^{20}$ 1.2644) until the reaction ceased. Seventy two grams of unreacted vinyl chloride was isolated from the reaction mixture along with 30.2 g of dimethylamide of phosphorodichloridic acid and 14.4 g (23%) of a substance which boiled, after two distillations, at 114-115° (1.5 mm); $d_4^{20}$ 1.4036; $n_D^{20}$ 1.4780.

Found %: C 20.25, 20.50; H 4.03, 4.04; N 6.73, 6.41. $C_4H_9ONPCl_3$. Calculated %: C 21.40; H 4.04; N 6.23.

b) The chloride of N,N-dimethyl-dichloroethylphosphonamidic acid, prepared from the chloride of dichloroethylphosphonic acid [2] and dimethylamine, boiled at 118° (2.5 mm); $d_4^{20}$ 1.3997; $n_D^{20}$ 1.4775.

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* Prepared by oxidative chlorophosphonation of vinyl chloride with phosphorus trichloride [2].

**4. Preparation of the ethyl ester of N,N-dimethyl-dichloroethylphosphonamidic acid.** To the solution of 7.1 g (0.035 mole) of the chloride of N,N-dimethyl-dichloroethylphosphonamidic acid in 50 ml of dry ether there was added 2.4 g (0.035 mole) of sodium ethoxide in 20 ml of ether. Five ml of water was added to the reaction mixture to dissolve the precipitated salt. There was isolated 1.4 g (17%) of the substance with:

B.p. 85-90° ( $1 \cdot 10^{-5}$ mm ); $d_4^{20}$ 1.2191; $n_D^{20}$ 1.4495; $MR_D$ 51.83; calculated $MR_D$ 51.80.

Found %: $C_2H_5O$ 18.48, 1819. $C_6H_{14}O_2Cl_2NP$. Calculated %: $C_2H_5O$ 19.25.

## SUMMARY

1. It has been shown that in oxidative chlorophosphonation of hydrocarbons and their derivatives one may employ as phosphonating agents the products of replacement of chlorine in phosphorus trichloride, these having the type $RXPCl_2$, where the hydrocarbon residue is bound to the phosphorus atom by a third element X.

2. Oxidative chlorophosphonation of cyclohexane by ethyl phosphorodichloridite and of vinyl chloride by methyl phosphorodichloridite and dimethylaminophosphorodichloridite was realized.

3. The chloride and the ethyl ester of N,N-dimethylamido-dichloroethylphosphonamidic acid, dimethyl ester of dichloroethylphosphonic acid and methyl ester of dichloroethylphosphonochloridic acid have been synthesized.

## LITERATURE CITED

[1] L. Z. Soborovskii, Iu. M. Zinov'ev and M. A. Englin, Doklady Akad. Nauk SSSR 67, 273 (1949); L. Z. Soborovskii and Iu. M. Zinov'ev, J. Gen. Chem. 24, 580 (1954); * Iu. M. Zinov'ev and L. Z. Soborovskii, J. Gen. Chem. 26, 3030 (1956).*

[2] L. Z. Soborovskii, Iu. M. Zinov'ev and L. I. Muler, Doklady Akad. Nauk SSSR, 109, 98 (1956).*

[3] B. A. Arbuzov and D. Kh. Yarmukhametova, Doklady Akad. Nauk SSSR, 101, 675 (1955).

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* Original Russian pagination. See C. B. Translation.

# TETRAACYLOXYSILANES IN ORGANIC SYNTHESIS

## XV. SYNTHESIS OF α, β-UNSATURATED ACIDS OF THE FURAN AND THIOPHENE SERIES

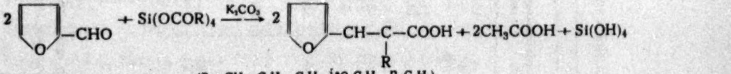
Iu. K. Iur'ev, G. B. Eliakov and A. N. Vysokosov

In our previous work [1] we showed that in the synthesis of cinnamic acid and its homologs (α-alkyl-β-phenylacrylic acids) by the Perkin reaction the silicoanhydrides of saturated monobasic acids (tetraacyloxysilanes) can successfully take the place of acid anhydrides in the condensation with benzaldehyde. It was therefore of interest to condense tetraacyloxysilanes with other aldehydes with an aromatic character – furfural and thiophene-2-aldehyde – in order to prepare β-(furyl-2)- and β-(thienyl-2)-acrylic acids.

According to the data of Marckwald [2] β-(furyl-2)-acrylic acid is obtained in good yield (80%) by the normal Perkin reaction from furfural and acetic anhydride in presence of potassium acetate.

The literature contains no information about the preparation of α-methyl-α-propyl- and α-butyl-β-(furyl-2)-acrylic acids by the Perkin reaction. Baeyer [3] and Carter [4] obtained α-ethyl-β-(furyl-2)-acrylic acid in 80% yield by condensation of furfural with butyric anhydride in presence of sodium butyrate. Schaarschmidt and co-workers[5] only obtained a negligible yield of α-isopropyl-β-(furyl-2)-aorylic acid (0.5%) on condensing furfural with isovaleric anhydride in presence of sodium isovalerate. Their main product (45%) was 3-methyl-1-(furyl-2)-1-butene (furylisoamylene), apparently the result of decarboxylation of the intermediate product of condensation as in the analogous condensation with benzaldehyde [6].

In the present work we studied the condensation of furfural with silicoanhydrides of acetic, propionic, butyric, valeric, isovaleric and caproic acids and we obtained β-(furyl-2)acrylic and (respectively) α-methyl-, α-ethyl, α-propyl-, α-isopropyl- and α-butyl-β-(furyl-2)-acrylic acids, thereby demonstrating that the field of application of tetraacyloxysilanes in organic synthesis can be still further widened.



(R = $CH_3$, $C_2H_5$, $C_3H_7$, iso-$C_3H_7$, n-$C_4H_9$).

Condensation of furfural with silicoacetic anhydride proceeds best of all in presence of potassium acetate, and the maximum yield of β-(furyl-2)-acrylic acid (59%) is reached with a molar ratio of components equal to 1 : 1.2 : 1 and with 10-hours' heating at 150-155°; the yield of acid fell to 53% when the heating period was reduced to 5 hours; prolongation of the heating period to 15 hours led to greater resinification and to a fall in yield of the acid to 45%. The acid yield was 52% when heating at 180° was carried out for 3 hours. The yield did not exceed 26% if postassium carbonate was used as condensing agent.

On the other hand, the condensation of furfural with silicoanhydrides of propionic and butyric acids in presence of potassium carbonate led to yields of 70.5% of α-methyl-β-(furyl-2)-acrylic acid and 60% of α-ethyl-β-(furyl-2)-acrylic acid respectively. Condensation of furfural with silicoanhydrides of valeric and caproic acids gave α-propyl and α-butyl-β-(furyl-2)-acrylic acids in the lower yields of 33 and 26% respectively. A very low yield of α-isopropyl-β-(furyl-2)-acrylic acid (3.3%) resulted from condensation of furfural with silicoisovaleric anhydride, but this was undoubtedly due to the above-noted secondary process of decarboxylation of the intermediate product of this condensation.

Reaction of Silicoanhydrides of Carboxylic Acids with Furfural and Thiophene-2-aldehyde

| Reaction components (in g) | | | | | Reaction conditions | | Reaction products | | | | | | | | Melting points reported in the literature |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Acid anhydride | | | | | | | | Yield | | Constants and analytical data | | | | | |
| | | | | | | | | | | | % C | | % H | | |
| Name | Quantity | furfural | potassium acetate | potassium carbonate | temperature | duration of heating (hrs) | Acid | in g | in % of theory | Melting point | found | calc. | found | calc. | |
| Silicoacetic anhydride | 26.4 | 9.6 | — | 13.8 | 145—150° | 5 | β-(Furyl-2)-acrylic | 3.6 | 26.0 | 140—141° * | — | — | — | — | 140° [2] |
| | 33.0 | 9.6 | 9.8 | — | 150—155 | 10 | | 8.1 | 59.0 | 140—141 * | — | — | — | — | 141 [9] |
| | 26.4 | 9.6 | 9.8 | — | 150—155 | 5 | | 7.3 | 53.0 | 140—141 * | — | — | — | — | |
| Silicopropionic | 32.0 | 9.6 | — | 13.8 | 155—160 | 10 | α-Methyl-β-(furyl-2)-acrylic | 10.7 | 70.5 | 115.5—116.2 | 63.26, 63.29 | 63.15 | 5.43, 5.46 | 5.30 | 116 [10] |
| | 32.0 | 9.6 | — | 13.8 | 155—160 | 5 | | 6.2 | 41.0 | 115.6—116.2 | — | — | — | — | |
| Silicobutyric | 22.0 | 4.8 | — | 6.9 | 100 | 30 | α-Ethyl-β-(furyl-2)-acrylic | 5.0 | 60.0 | 98.5—99 | 65.14, 65.10 | 65.05 | 6.09, 6.04 | 6.06 | 95.5—97 [3] |
| | 37.6 | 9.6 | — | 13.8 | 100 | 15 | | 5.9 | 36.0 | 98.5—99 | — | — | — | — | |
| | 19.0 | 4.8 | — | 6.9 | 165—170 | 5 | | 3.7 | 44.5 | 98.5—99 | — | — | — | — | |
| Silicovaleric | 11.0 | 2.4 | — | 3.5 | 145—150 | 8 | α-Propyl-β-(furyl-2)-acrylic | 1.5 | 33.0 | 100—101 | 66.53, 66.61 | 66.65 | 6.72, 6.69 | 6.71 | Not described in the literature |
| Silicoisovaleric | 43.0 | 9.6 | — | 13.8 | 120—125 | 15 | α-Isopropyl-β-(furyl-2)-acrylic | 0.6 | 3.3 | 114—114.5 | 66.50, 66.59 | 66.65 | 6.79, 6.79 | 6.71 | 114 [3] |
| Silicocaproic | 49.0 | 9.6 | — | 13.8 | 155—160 | 10 | α-Butyl-β-(furyl-2)-acrylic | 5.1 | 26.0 | 73.8—74.2 | 68.05, 68.08 | 68.01 | 7.29, 7.31 | 7.26 | Not described in the literature |
| | | Thiophene-2-aldehyde | | | | | | | | | | | | | |
| Silicoacetic anhydride | 17.0 | 5.6 | 4.9 | — | 150—155° | 10 | β-(Thienyl-2)-acrylic | 1.9 | 25.0 | 144.5—145** | — | — | — | — | 138 [7] |
| | 18.0 | 3.36 | 5.1 | — | 170—175 | 10 | | 3.7 | 80.0 | 144.5—145 | — | — | — | — | 144—145 [11] |

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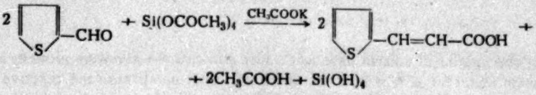
* No depression observed in mixed melting test with authentic β-(furyl-2)acrylic acid.

** No depression observed in mixed melting test with authentic β-(thienyl-2)-acrylic acid; 3.25 g (58%) of unchanged thiophene-2-aldehyde with b.p. 196-198° was also isolated.

In the present work we also studied the condensation of thiophene-2-aldehyde with silicoacetic anhydride, which gave β-(thienyl-2)-acrylic acid. The latter was described by Biderman [7] who prepared it by condensation of thiophene-2-aldehyde with acetic anhydride in presence of potassium acetate at the boil, but did not state the yield.

We found that condensation of thiophene-2-aldehyde with silicoacetic anhydride in presence of potassium acetate calls for more drastic conditions than are needed in the corresponding condensation of furfural. Under the conditions most favorable for condensation of furfural, the yield of β-(thienyl-2)-acrylic acid was only 25%, and 58% of the aldehyde was recovered unchanged, whereas heating to 170-175° for 10 hours increased the acid yield to 80%.



## EXPERIMENTAL

The previous procedure [1] was employed for preparation of silicoanhydrides of saturated monobasic acids, for their condensation with furfural and with thiophene-2-aldehyde (b.p. 80° at 12 mm, 198° at 756 mm, $n_D^{20}$ 1.5889, $d_4^{20}$ 1.224 [8]), as well as for isolation of the reaction products (see table for results obtained).

## SUMMARY

The possibility of application of silicoanhydrides of saturated monobasic organic acids for synthesis of α, β unsaturated acids of the furan and thiophene series was demonstrated by preparations of β-(furyl-2)- and α-alkyl-β-(furyl-2)-acrylic acids, as well as of β-(thienyl-2)-acrylic acid, by condensation of furfural and thiophene-2-aldehyde with the appropriate silicoanhydrides.

## LITERATURE CITED

[1] Iu. K. Iur'ev, G. B. Eliakov and A. N. Vysokosov, J. Gen. Chem. 26, 926 (1956).*

[2] W. Marckwald, Ber. 20, 2812 (1887).

[3] A. Baeyer, Ber. 10, 357 (1877).

[4] A. Carter, J. Am. Chem. Soc. 50, 2299 (1928).

[5] A. Schaarschmidt, E. Georgeacopol and J. Herzenberg, Ber. 51, 1059 (1918).

[6] D. Breslow and C. Hauser, J. Am. Chem. Soc. 61, 786, 793 (1939).

[7] A. Biderman, Ber. 19, 1856 (1886).

[8] E. Campaigne and W. Arche, J. Am. Chem. Soc. 75, 989 (1953).

[9] J. Jonson, Org. Synth. 20, 55 (1940).

[10] J. Kasiwagi, Bull. Chem. Soc. Japan. 2, 310 (1927); Zbl. 1928, I, 690.

[11] R. Cohn, Ber. 25, 2459 (1892).

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# THE CHLORINATION OF n-HEXANE AND n-HEPTANE

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Processes of chlorination of alkanes have repeatedly attracted the attention of many investigators in the search for convenient routes for passage from the chemically inert paraffins to the reactive halogenated derivatives. The great interest in the field of photochemical chlorination of hydrocarbons is due mainly to the possibility of successful application of the process at low temperatures with a higher degree of conversion and with a high productivity per unit of reaction space. No less interesting is the catalytic chlorination of alkanes.

The literature is lacking in any data about chlorination of higher alkanes beyond the first five members of the series.

Lemke and Tishchenko [1] carried out the photochemical chlorination of n-pentane in the liquid phase and obtained 60% of dichlorides, 28-34% of monochlorides and 7-8% of trichlorides.

E. T. McBee and H. B. Hass [2] carried out the photochemical chlorination of n-butane, isobutane, n-pentane and isopentane.

A. V. Topchiev, B. A. Krentsel and L. N. Andreev [3] studied the photochemical chlorination of n-butane in a flow apparatus. Use has also been made [4] of series of heterogeneous catalysts for the chlorination of n-butane, an iron catalyst was found to be the most active. B. A. Krentsel and N. A. Pokotilo [5] chlorinated n-butane in presence of active carbon and Askanite* in the pure form or impregnated with copper chloride. A number of authors [6-11] chlorinated higher alkanes in presence of active carbon, silica gel and chlorides of some metals.

In the present work we studied the photochemical chlorination of n-heptane and the catalytic chlorination of n-hexane and n-heptane.

Photochemical chlorination of heptane was found to give dichloropentanes in high yield. The most active of the catalysts tested was cobalt chloride deposited on pumice. Its high activity is probably due to its ability to initiate chain growth (development of free radicals).

$$CoCl_2 \longrightarrow CoCl + Cl$$

$$CoCl + Cl + C_6H_{14} \longrightarrow HCoCl_2 + C_9H_{13}$$

$$HCoCl_2 \xrightarrow{\text{heating}} CoCl + HCl$$

$$CoCl + Cl_2 \longrightarrow CoCl_2 + Cl$$

$$Cl + C_6H_{13} \longrightarrow C_6H_{13}Cl$$

The intially formed hexyl chloride can react with elemental chlorine to form 1,6-dichlorohexane [12].

## EXPERIMENTAL

### Photochemical Chlorination

The initial n-heptane had b.p. 98.4° (754 mm), $d_4^{20}$ 0.6843, $n_D^{20}$ 1.3879.

Chlorination was performed in the apparatus illustrated in the diagram.

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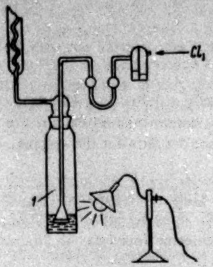
* As in original – Publisher's note.



Set-up for photochlorination of hydrocarbons.

Hydrocarbon in reactor 1 was irradiated with an electric lamp. Chlorine from a cylinder passed through a drying bottle (containing sulfuric acid) and a flowmeter and entered the reactor through a capillary tube or a porous glass filter. The light source was an electric lamp (200 watt) which during the first 15 minutes of the experiment was placed at a distance of 5 cm from the reactor and subsequently at a distance of 14 cm.

Experiments were run with various volumetric ratios of hydrocarbon to chlorine. The latter was admitted at a rate of 0.76 liter/hour. Results of the best experiments are shown in Table 1. The latter shows that increase in the amount of chlorine is accompanied by a fall in yield of dichlorides.

31.2 g of condensate from experiment 2 was washed and dried before being subjected to careful fractionation. The following fractions were obtained:

1st, b.p. 146-148° (754 mm), $d_4^{20}$ 0.8672, $n_D^{20}$ 1.4222; chlorine content found %: 26.4; calculated %: 26.34; 2nd, b.p. 159-161° (754 mm), $d_4^{20}$ 0.8726, $n_D^{20}$ 1.4284; chlorine content found %: 26.4; calculated %: 26.34; 3rd, b.p. 119-120° (28 mm), $d_4^{20}$ 1.0980, $n_D^{20}$ 1.4707; chlorine content found %: 42.50; calculated %: 42.47.

TABLE 1

Photochemical Chlorination of n-Heptane in the Liquid Phase with Dry Chlorine at 14-16°

| Expt. No. | Chlorine taken (liters) | Molar ratio of n-heptane to chlorine | Yield of condensate (g) | Composition of condensate (%) | | | |
|---|---|---|---|---|---|---|---|
| | | | | monochlorides | | dichlorides | polychlorides |
| | | | | secondary | 1-chloroheptane | | |
| 1 | 10.9 | 1 : 1 | 28.6 | 12.3 | 11.5 | 76.2 | — |
| 2 | 21.8 | 1 : 2 | 31.2 | 10.2 | 9.7 | 80.0 | — |
| 3 | 27.3 | 1 : 2.2 | 31.5 | 4.3 | 4.5 | 74.9 | 16.3 |
| 4 | 32.7 | 1 : 3 | 31.9 | — | — | 61.6 | 36.4 |

Note. 21.6 g of n-heptane was consumed in each experiment in 4 hours.

On the basis of comparison with literature data [12], we see that the 1st fraction corresponds to 2-chloroheptane, the 2nd to 1-chloroheptane and the 3rd to 1,7-dichloroheptane.

In subsequent experiments the proportion of chlorine was increased by a factor of 3 and the reaction period to 6.5 hours. The reaction product consisted solely of polychlorides; mono- and dichlorides could not be detected.

## Catalytic Chlorination of n-Hexane and n-Heptene

Characteristics of starting hydrocarbons. n-Hexane: b.p. 68.7° (754 mm), $d_4^{20}$ 0.6594, $n_D^{20}$ 1.3749 n-Heptane: b.p. 98.4° (754 mm), $d_4^{20}$ 0.6837, $n_D^{20}$ 1.3877.

Experiments were performed in a flow apparatus. The action of the following catalysts was investigated: active carbon, aluminum chloride on active alumina, ferric chloride on wood charcoal, asbestos and pumice, nickel chloride on pumice, copper chloride on pumice, magnesium chloride on pumice and on magnesia, barium chloride on magnesia, cobalt chloride on silica gel active alumina, potsherds and pumice. All of the catalysts (except aluminum chloride on alumina) contained 15% of metal chlorides, and they were tested for catalytic activity under standard conditions: temperature 320°, catalyst volume

100 ml, molar ratio of hydrocarbon to chlorine 1 : 2, space velocity for n-hexane 0.17 and for n-heptane 0.18, chlorine flow rate 0.55 liter/hour.

The first series of hexane chlorinations $C_6H_{14} + 2Cl_2 \rightarrow C_6H_{12}Cl_2 + 2HCl$ were carried out with the aim of selection of the best catalyst at 320°.

After they had been washed and dried, the catalyzates were fractionally distilled in a 40-plate column. The fractions were analyzed for chlorine content and their composition was determined on the basis of the analytical data and the physicochemical constants. As an example, we present the data for the condensate from experiment 19.

Fractions obtained: 1st, b.p. 122-124° (758 mm), $d_4^{20}$ 0.8732, $n_D^{20}$ 1.4136; chlorine found %: 29.58; calculated %: 29.4; 2nd, b.p. 134-136° (758 mm), $d_4^{20}$ 0.8780, $n_D^{20}$ 1.4232; chlorine found %: 29.53; calculated %: 29.4; 3rd, b.p. 93.0-94.5° (22 mm), $d_4^{20}$ 1.086, $n_D^{20}$ 1.4570; chlorine found %: 45.78; calculated %: 45.74.

TABLE 2

Catalytic Chlorination of n-Hexane in the Vapor Phase

| Expt. No. | Catalysts | Yield of condensate (%) | Unreacted hydrocarbon (%) | Composition of condensate (in %) calculated on hydrocarbon reacted | | | |
|---|---|---|---|---|---|---|---|
| | | | | sec. chlorides | 1-chlorohexane | dichlorides | polychlorides |
| 5 | Active carbon | 10.5 | 91.9 | 8.1 | — | — | — |
| 6 | Aluminum chloride (3%) on active alumina | 10.6 | 66.6 | 33.4 | — | — | — |
| 7 | Ferric chloride on wood charcoal | 12.5 | 90.0 | 5.2 | 3.8 | — | — |
| 8 | Ferric chloride on asbestos | 12.3 | 41.9 | 55.3 | 2.8 | — | — |
| 9 | Ferric chloride on pumice | 14.2 | 11.5 | 69.2 | 19.3 | — | — |
| 10 | Nickel chloride on pumice | 8.5 | 53.2 | 46.8 | — | — | — |
| 11 | Cupric chloride on pumice | 10.5 | 63.0 | 18.3 | 15.9 | — | — |
| 12 | Magnesium chloride on pumice | 12.9 | 65.8 | 62.5 | 21.6 | — | — |
| 13 | Magnesium chloride on magnesia | 12.7 | 63.0 | 37.0 | — | — | — |
| 14 | Barium chloride on magnesia | 12.8 | 72.4 | 27.6 | — | — | — |
| 15 | Cobalt chloride on silica gel | 10.9 | 22.2 | 75.3 | 2.5 | — | — |
| 16 | Cobalt chloride on active alumina | 11.0 | 83.5 | 16.5 | — | — | — |
| 17 | Cobalt chloride on potsherds | 14.9 | 83.0 | 51.6 | 8.5 | 23.0 | 12.0 |
| 18 | Cobalt chloride on pumice | 15.2 | 60.7 | 2.5 | 4.7 | 53.5 | — |
| 19 | Pumice | 14.9 | 9.8 | 56.0 | 5.5 | 18.7 | 9.0 |

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Note. 10.8 g hexane and 5.45 g chlorine were taken in each experiment.

Comparison of the properties of the fractions with the literature data shows that the 1st fraction is a mixture of secondary chlorides, the properties of the 2nd fraction resemble those of 1-chloroheptane, and those of the 3rd fraction resemble those of 1,6-dichlorohexane.

Data obtained for various catalysts are included in Table 2 for comparison of their activities under standard conditions. It appears that cobalt chloride deposited on granular pumice is the best catalyst. This catalyst was in use for 170 hours without loss of activity.

Catalytic chlorination of n-heptane was likewise carried out at 330-340° in presence of $CoCl_2$ on pumice under standard conditions. The catalyzates were washed and dried before being fractionated in a vacuum-column The following fractions were obtained:

1st, b.p. 46° (19.5 mm), $d_4^{20}$ 0.8670, $n_D^{20}$ 1.4220; chlorine found %: 26.43; calculated %: 26.34; 2nd, b.p. 63° (27 mm), $d_4^{20}$ 0.8726, $n_D^{20}$ 1.4284; chlorine found %: 26.41; calculated %: 26.34; 3rd, b.p. 119-120° (28 mm), $d_4^{20}$ 1.098, $n_D^{20}$ 1.4707; chlorine found %: 42.5; calculated %: 42.47.

The 1st fraction corresponded to 2-chloroheptane, and the 2nd and 3rd were assumed to be 1-chloroheptane and 1,7-dichloroheptane, respectively. The yield of the 1,7-dichloroheptane fraction was 32% calculated on the reacted n-heptane. The determined constants are in agreement with the literature data [12].

## SUMMARY

1. Photochemical chlorination of n-heptane in the liquid phase was studied and the conditions for preparation of dichloropentanes in good yields were established. The need for thorough dispersion of the chlorine during photochemical chlorination of alkanes was demonstrated.

2. The catalytic properties of chlorides of various metals in the chlorination of alkanes were studied.

3. Cobalt chloride deposited on pumice was found to be the most efficient of the catalysts examined.

## LITERATURE CITED

[1] A. Lemke and D. V. Tishchenko, J. Gen. Chem. 7, 1995 (1937).

[2] E. T. McBee and H. B. Hass, Ind. Eng. Ch. 29, 305 (1947).

[3] A. V. Topchiev, B. A. Krentsel and L. N. Andreev, Proc. Acad. Sci. USSR 85, 1049 (1952).

[4] B. A. Krentsel', Principles of Synthesis of Aliphatic Alcohols from Petroleum Hydrocarbons [in Russian] (Acad. Sci. USSR Press, 1954), p. 101.

[5] B. A. Krentsel' and N. A. Pokotilo, J. Appl. Chem. 14, 727 (1951). •

[6] German Patent 436999 (1926).

[7] M. Giordani, Ann. chim. appl., 25, 163 (1935).

[8] U.S. Patent 2140547 (1938).

[9] Iu. G. Mamedaliev et al., J. Appl. Chem. 12, 1826 (1939).

[10] L. H. Reyerson and S. Vuster, J. Phys. Chem., 39, 1111 (1935).

[11] V. A. Nekrasova and N. D. Zelinskii, Author's Certificate No. 95247 (1953); V. A. Nekrasova, Proc. Acad. Sci. USSR, 88, 475 (1953).

[12] R. H. Clark and H. R. Streight, Chem. A., 24, 586 (1930); A. I. Vogel, J. Chem. Soc., 1943, 536.

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•Original Russian pagination. See C.B. Translation.

# THE PROBLEM OF THE PRODUCTION OF ALIPHATIC ALCOHOLS FROM PETROLEUM HYDROCARBONS

V. A. Nekrasova

The problem of the production of $C_6$-$C_{12}$ aliphatic alcohols from petroleum hydrocarbons via their chlorination products is not discussed at all in the literature, although the hydrolysis of the lower chloroalkanes has been studied fairly closely.

Studies have been made, for example, the hydrolysis of isoamyl chloride at 170-180° which gives a 28% yield of isoamyl alcohol [1, 2]. Confirmation of these results was later obtained [3].

Liquid-phase hydrolysis of butyl chloride with milk of lime in an autoclave gave an 80% yield of primary n-butyl alcohol [4, 5].

With the objective of hydrolyzing $C_6$-$C_{12}$ chloroalkanes we made use of chlorides synthesized from n-alkanes isolated from gasoline by straight-running of Crimean oil, the paraffinic portion of which consists almost exclusively of alkanes of normal structure. Other Black Sea oils (Il'sk and Khadyzhensk) have approximately the same composition.

## EXPERIMENTAL

Hydrocarbons of normal structure were separated from isomers and cyclic hydrocarbons by formation of urea complexes [6]. They were then subjected to fine rectification in a 70-plate column. The properties of the isolated hydrocarbons are presented in Table 1.

TABLE 1

Properties of n-Alkanes Isolated from Gasoline from Crimean Oil

| Hydrocarbons | Boiling point (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ |
|---|---|---|---|
| n-Hexane | 68— 69° (751) | 0.6594 | 1.3750 |
| n-Heptane | 98— 99 (754) | 0.6838 | 1.3878 |
| n-Octane | 125—126 (754) | 0.7026 | 1.3975 |
| n-Nonane | 150—151 (751) | 0.7177 | 1.4054 |
| n-Decane | 174—175 (750) | 0.7298 | 1.4120 |
| n-Undecane | 195—196 (757) | 0.7403 | 1.4172 |
| n-Dodecane | 215.5—217 (755) | 0.7489 | 1.4218 |

We performed the vapor-phase thermal chlorination of n-alkanes in presence of nitrogen dioxide [7].

The prepared chlorides were washed with water, sodium carbonate solution, and again with water, dried with anhydrous calcium chloride, and subjected to fine rectification in a 40-plate, glass-packed column. The chlorine content of the chloroalkanes was determined by double combustion [8].

The properties of the monochloro derivatives are presented in Table 2.

The primary $C_6$-$C_{12}$ monochlorides were hydrolyzed in a stainless steel, rotating autoclave. Optimum conditions of hydrolysis were estabished in preliminary experiments and were employed in the subsequent hydrolysis of the other chloroalkanes.

TABLE 2

Physicochemical Properties of the Isolated Primary Monochlorides

| Chloroalkanes | Boiling point (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ | | Chlorine content (%) | |
|---|---|---|---|---|---|---|---|
| | | | | found | calc. | found | calc. |
| 1-Chlorohexane | 135—137° (758) | 0.8760 | 1.4236 | 35.0 | 35.04 | 29.53 | 29.19 |
| 1-Chloroheptane | 159—161 (756) | 0.8726 | 1.4284 | 39.36 | 39.40 | 26.62 | 26.37 |
| 1-Chlorooctane | 183—185 (757) | 0.8709 | 1.4311 | 44.15 | 44.01 | 23.98 | 23.88 |
| 1-Chlorononane | 202—204 (755) | 0.8702 | 1.4360 | 48.61 | 48.63 | 21.96 | 21.82 |
| 1-Chlorodecane | 222—224 (754) | 0.8697 | 1.4380 | 53.29 | 53.25 | 20.34 | 20.09 |
| 1-Chloroundecane | 240—242 (754) | 0.8692 | 1.4399 | 57.83 | 57.86 | 18.85 | 18.59 |
| 1-Chlorododecane | 255—257 (758) | 0.8686 | 1.4418 | 62.39 | 62.48 | 17.79 | 17.25 |

As an example we give the results of hydrolysis of 1-chloroheptane: 100 g 1-chloroheptane was charged into the 1-liter autoclave followed by 233 ml 20% sodium hydroxide solution and 50 g emulsifying agent (product of sulfochlorination of heavy fractions of Synthine). The autoclave was thereupon heated to 170-175° while being rotated at a constant speed of 150 revs. per min. During this operation the pressure in the autoclave rose to 20-25 atm. At the termination of the experiment, the upper layer was separated from the reaction mass and acidified with 20% sulfuric acid. The resulting alcohol was distilled off in steam together with unreacted haloalkane and unsaturated hydrocarbon.

The isolated crude product was washed with sodium carbonate solution and water, thoroughly dried with calcined potassium carbonate, and subjected to fine fractionation. Yield of heptyl alcohol 61.26 g (80%), b.p. 176-177° (755 mm), $d_4^{20}$ 0.8218, $n_D^{20}$ 1.4241.

The properties of the other prepared alcohols are presented in Table 3.

TABLE 3

Physicochemical Properties of the Isolated Primary Aliphatic Alcohols

| Alcohols | Boiling point (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ | |
|---|---|---|---|---|---|
| | | | | found | calculated |
| n-Hexyl | 155—156° (754) | 0.8185 | 1.4179 | 31.45 | 31.43 |
| n-Heptyl | 176—177 (755) | 0.8218 | 1.4241 | 36.09 | 36.05 |
| n-Octyl | 195—196 (754) | 0.8245 | 1.4292 | 40.74 | 40.67 |
| n-Nonyl | 215—216 (753) | 0.8273 | 1.4334 | 45.35 | 45.29 |
| n-Decyl | 229—230 (754) | 0.8291 | 1.4368 | 49.99 | 49.91 |
| n-Undecyl | 146—147 (25) | 0.8354 | 1.4404 | 54.40 | 54.52 |
| n-Dodecyl | 149—150 (20) | 0.8372 | 1.4439 | 59.11 | 59.14 |

## SUMMARY

1. The possibility of synthesis of primary aliphatic alcohols fron the corresponding alkanes via their chlorination products was studied.

2. Optimum conditions were established for hydrolysis of the primary chloroalkanes in 75-80% yield.

## LITERATURE CITED

[1] S. S. Nametkin, Selected Works [in Russian] (Acad. Sci. USSR Press, 1949), p. 676.

[2] S. S. Nametkin and Kh. G. Serebrennikova, J. Appl. Chem., 9, 1423 (1936); Bull. Acad. Sci. USSR, Div. Tech. Sci., 1944, No. 1.

[3] A. S. Nekrasov and A. A. Nagatkina, Bull. Acad. Sci. USSR, Div. Tech. Sci., 1947, 803.

[4] B. A. Krentsel', Chemical Utilization of Petroleum Hydrocarbon Gases [in Russian] (Acad. Sci. USSR Press, 1952), p. 92.

[5] B. A. Krentsel' and L. M. Tolchinskii, J. Appl. Chem., 23, 1051. (1950).*

[6] W. Z. Zimmerschied and B. A. Dinerstein, Ind. Eng. Ch., 42, 1300 (1950).

[7] V. A. Nekrasova and N. I. Shuikin, Proc. Acad. Sci. USSR, 97, 843 (1954);* Bull. Acad. Sci. USSR, Div. Chem. Sci., 1956, 583.*

[8] N. P. Volynskii and I. K. Chudakova, Trans. Inst. Pet., USSR, 8, 88 (1956).

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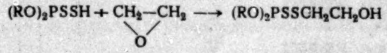
# REACTION OF DIALKYL DITHIOPHOSPHATES WITH ETHYLENE SULFIDE

T. A. Mastriukova, V. N. Odnoralova and M. I. Kabachnik

Some time ago we published an article about the addition of dialkyl dithiophosphates to ethylene oxide [1]. As shown in that paper, these substances react smoothly with formation of $\beta$-hydroxy-substituted esters dithiophosphoric acid.



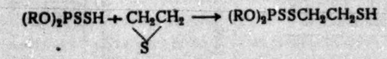
$$(RO)_2PSSH + \underset{O}{CH_2{-}CH_2} \longrightarrow (RO)_2PSSCH_2CH_2OH$$

The present study is devoted to the examination of the reaction of dialkyl dithiophosphates with ethylene sulfide.

As is known [2-4], ethylene sulfide is a rather reactive compound which resembles ethylene oxide in many reactions. Thus, mercaptans, phenols, and amines add to ethylene sulfide with opening of its three-membered ring [3-6]. Under the action of aqueous solutions of bases – alkali, pyridine, diethylamine – there takes place a rapid polymerization of ethylene sulfide [2, 4, 8]. As to acids, those like sulfuric and acetic cause polymerization of the ethylene sulfide [2, 7]; hydrogen chloride and hydrogen sulfide, on the other hand, add to ethylene sulfide [2, 3]. Addition of hydrogen chloride also takes place under the action of concentrated hydrochloric acid [2].

Dialkyl dithiophosphates are strong acids with ionization constants of the order of $10^{-2}$ in water [9]. Therefore one might presuppose that they would cause the polymerization of ethylene sulfide. On the other hand one might expect their addition with opening of the three-membered ring, analogous to that of addition of hydrogen sulfide and hydrogen chloride. In the latter case the reaction would proceed analogously to the addition of dialkyl dithiophosphates to ethylene oxide.

The study showed that dialkyl dithiophosphates add to ethylene sulfide with formation of dialkyl S-$\beta$-mercaptoethyl dithiophosphates.



$$(RO)_2PSSH + \underset{S}{CH_2CH_2} \longrightarrow (RO)_2PSSCH_2CH_2SH$$

In contrast to ethylene oxide this addition occurs under more drastic conditions: thus while ethylene oxide reacts at room temperature, ethylene sulfide forms the addition product only after being heated.

In Table 1 are given the constants and the analyses of the dialkyl S-$\beta$-mercaptoethyl dithiophosphates prepared by us. These are colorless liquids which are unstable thermally. They are readily soluble in organic solvents but are insoluble in water. They are decomposed by alkalies analogously to dialkyl $\beta$-hydroxyethyl dithiophosphates.

The sulfhydryl group of $\beta$-mercaptoethyl dithiophosphates is readily acetylated. Thus, from dialkyl S-$\beta$-mercaptoethyl dithiophosphates there were prepared the corresponding acetyl derivatives by the reaction with acetic anhydride in the presence of pyridine:

TABLE 1

Dialkyl S-β-Mercaptoethyl Dithiophosphates and Their Derivatives.

| Ordinal No. | Formula | Boiling point (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | Yield (%) | Analyses(in %) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | C | | H | | P | | S | |
| | | | | | | found | calc. | found | calc. | found | calc. | found | calc. |
| 1 | $(CH_3O)_2PSSCH_2CH_2SH$ | 105—106° (1) | 1.5690 | 1.2882 | 60 | 22.17, 22.06 | 22.01 | 5.04, 5.03 | 5.08 | 13.76, 13.90 | 14.19 | 43.82, 43.92 | 44.07 |
| 2 | $(C_2H_5O)_2PSSCH_2CH_2SH$ | 110—112 (1.5) | 1.5438 | 1.1966 | 64 | 29.59, 29.47 | 29.25 | 6.17, 6.11 | 6.13 | 12.40, 12.40 | 12.57 | 39.00, 38.76 | 39.04 |
| 3 | $(C_3H_7O)_2PSSCH_2CH_2SH$ | 113—115 (1) | 1.5312 | 1.1424 | 46 | 35.61, 35.50 | 35.01 | 6.99, 6.99 | 6.98 | 10.92, 10.80 | 11.29 | 34.83, 34.61 | 35.05 |
| 4 | $(isoC_3H_7O)_2PSSCH_2CH_2SH$ | 110—112 (1.5) | 1.5230 | 1.1287 | 44 | 35.49, 35.56 | 35.01 | 7.01, 7.02 | 6.98 | 11.16, 11.36 | 11.29 | 35.00, 35.00 | 35.05 |
| 5 | $(iso\text{-}C_4H_9O)_2PSSCH_2CH_2SH$ | 129—131 (1.5) | 1.5198 | 1.0966 | 46 | — | — | — | — | 10.16, 10.40 | 10.24 | 31.94, 31.79 | 31.81 |
| 6 | $(C_2H_5O)_2PSSCH_2CH_2SCOCH_3$ | 135—137 (2.5) | 1.5351 | 1.1994 | 22 | 33.56, 33.49 | 33.32 | 6.11, 6.02 | 5.94 | 10.55, 10.58 | 10.74 | — | — |
| 7 | $(iso\text{-}C_4H_9O)_2PSSCH_2CH_2SCOCH_3$ | 143—144 (2.5) | 1.5170 | 1.1074 | 19 | 41.89, 42.09 | 41.83 | 7.38, 7.38 | 7.31 | 8.76, 8.85 | 8.82 | 28.29, 28.16 | 27.92 |
| 8 | $(C_2H_5O)_2PSSCH_2CH_2SCH_3$ * | 111—113 (1) | 1.5388 | 1.1708 | 51 | 32.56, 32.64 | 32.28 | 6.61, 6.60 | 6.58 | — | — | 36.43, 36.73 | 36.94 |
| 9 | $(C_3H_7O)_2PSSCH_2CH_2SCH_3$ | 128—129 (1.5) | 1.5270 | 1.1229 | 62 | 37.80, 38.01 | 37.47 | 7.36, 7.28 | 7.30 | 10.52, 10.71 | 10.74 | 33.18, 33.01 | 33.35 |
| 10 | $(iso\text{-}C_3H_7O)_2PSSCH_2CH_2SCH_3$ | 115 (1.5) | 1.5179 | 1.1087 | 62 | 37.20, 37.20 | 37.47 | 7.39, 7.36 | 7.34 | 10.50, 10.44 | 10.74 | 33.20, 33.04 | 33.35 |

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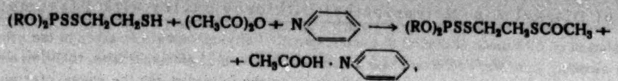
* Constants of substance No. 8 prepared previously [10]: b.p. 155-156° at 3 mm, $n_D^{20}$ 1.5405, $d_4^{20}$ 1.1699.

TABLE 2

Reactions of Ethylene Sulfide with Dialkyl Dithiophosphates

| Ordinal No. | Formula of reaction product | Am'ts of starting materials in moles | | Reaction conditions | | $n_D^{20}$ | $d_4^{20}$ | Analyses in % | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | acid | ethylene sulfide | temperature | time in hours | | | C | | H | | P | | S | |
| | | | | | | | | found | calc. | found | calc. | found | calc. | found | calc |
| 1 | $(CH_3O)_2PSSCH_2CH_2SH$ | 0.06 | 0.07 | 72—74° | 9.5 | 1.5738 | 1.2915 | 21.98, 21.80 | 22.01 | 4.84, 4.90 | 5.08 | 13.86, 14.15 | 14.19 | 43.77, 44.11 | 44.07 |
| 2 | $(C_2H_5O)_2PSSCH_2CH_2SH$ | 0.07 | 0.08 | 72—74 | 9.5 | 1.5485 | 1.2041 | 29.17, 29.39 | 29.25 | 6.04, 6.03 | 6.13 | 12.58, 12.57 | 12.57 | 39.11, 39.13 | 39.04 |
| 3 | $(C_3H_7O)_2PSSCH_2CH_2SH$ | 0.06 | 0.07 | 76—78 | 12 | 1.5370 | 1.1522 | 35.22, 65.29 | 35.01 | 6.92, 6.83 | 6.98 | — | — | 35.53, 35.44 | 35.05 |
| 4 | $(iso\text{-}C_3H_7O)_2PSSCH_2CH_2SH$ | 0.05 | 0.07 | 77—78 | 13 | 1.5365 | 1.1506 | 35.06, 35.06 | 35.01 | 6.88, 6.92 | 6.98 | 11.20, 11.05 | 11.29 | 34.48, 34.62 | 35.05 |
| 5 | $(iso\text{-}C_4H_9O)_2PSSCH_2CH_2SH$ | 0.045 | 0.06 | 75—80 | 14 | 1.5265 | 1.1088 | 39.87, 39.72 | 39.71 | 7.59, 7.47 | 7.59 | 10.07, 10.13 | 10.24 | 32.35, 32.34 | 31.81 |



the constants and the analyses of these products are shown in Table 1.

β-Mercaptoethyl dithiophosphates react with diazomethane in the presence of methyl alcohol; the sulfhydryl group is methylated thereby:

$$(RO)_2PSSCH_2CH_2SH + CH_2N_2 \longrightarrow (RO)_2PSSCH_2CH_2SCH_3 + N_2$$

Substances of this type have been known earlier [10]; they are effective systemic insecticides. Triethyl dithiophosphate was isolated as the main product in an attempt to conduct an alkylation of diethyl S-β-mercaptoethyl dithiophosphate with ethyl bromide in the presence of sodium carbonate. A polymer of ethylene sulfide formed along with the triethyl dithiophosphate when sodium hydroxide was employed in this reaction. Evidently the reaction may be represented by the following scheme:

$$n + 2(C_2H_5O)_2PSSCH_2CH_2SH + nC_2H_5Br + nNaOH \longrightarrow n(C_2H_5O)_2PS(SC_2H_5) + \\ + H_2S + nNaBr + nH_2O + (C_2H_5O)_2PSS(CH_2CH_2S)_{n+2}PS(OC_2H_5)_2$$

Similar reactions are known among esters of thiocarboxylic acids which contain a sulfhydryl group in the β-position [11].

## EXPERIMENTAL

The dialkyl dithiophosphates necessary for the reaction were prepared and purified according to the previously known methods [12]. We used for the reactions ethylene sulfide [4] which was stabilized with ethylmercaptan [13].

### Preparation of Dialkyl S-β-Mercaptoethyl Dithiophosphates

The mixture of the dialkyl dithiophosphate and ethylene sulfide was placed into a steel bomb with a glass liner. The sulfide was taken usually in slight excess. Then the bomb was heated to 70-80° for 9.5 to 14 hours, depending on the size of the radical of the dialkyl dithiophosphate used. The end of the reaction was determined by the absence of the acid test to Congo red in the reaction mixture. The excess ethylene sulfide was removed in vacuum and the residual almost colorless product was analyzed and its constants were determined. Then the crude product was distilled in vacuum in nitrogen atmosphere. In all cases the undistilled product was close to the distilled product in physical constants. In Table 2 are shown the data on the reaction of ethylene sulfide with dialkyl dithiophosphates, as well as the constants of the undistilled substances and their analyses; in Table 1 are shown the constants and analyses of the distilled substances.

### Acetylation of Dialkyl S-β-Mercaptoethyl Dithiophosphates

To a solution of dialkyl S-β-mercaptoethyl dithiophosphate in dry pyridine, acetic anhydride was added dropwise. The reaction proceeded with slight heat effect. After several hours the reaction mixture was decomposed with 5% acetic acid with cooling. The organic layer was separated, and the aqueous layer was extracted with ether. The combined extracts were washed with sodium carbonate and water. After drying over calcined sodium sulfate, the reaction mixture was fractionated.

Diethyl S-β-acetylmercaptoethyl dithiophosphate was prepared from 7.8 g (0.03 mole) of diethyl S-β-mercaptoethyl dithiophosphate and 4.3 g (0.04 mole) of acetic anhydride in 10 ml of pyridine; the constants and analyses are shown in Table 1.

Diisobutyl S-β-acetylmercaptoethyl dithiophosphate was prepared from 6.4 g (0.02 mole) of diisobutyl S-β-mercaptoethyl dithiophosphate and 3.4 g (0.03 mole) of acetic anhydride in 10 ml. of pyridine (see Table 1).

### Alkylation of Dialkyl S-β-Mercaptoethyl Dithiophosphates with Diazomethane

To the solution of 0.02 mole of dialkyl S-β-mercaptoethyl dithiophosphate in ether in the presence of 5 ml of methyl alcohol, there was added dropwise an ethereal solution of diazomethane, taken in excess. The formation of nitrogen was completed within 20-30 minutes. On the following day the excess diazomethane was removed, the ethereal solution was washed with sodium carbonate and water and was dried over sodium sulfate. After distillation of the ether, the reaction product was distilled in vacuum. The constants and analyses of the products are shown in Table 1.

### Alkylation of Diethyl S-β-Mercaptoethyl Dithiophosphate in the Presence of Sodium Carbonate

The mixture of 16.2 g (0.066 mole) of diethyl S-β-mercaptoethyl dithiophosphate, 9 g (0.082 mole) of ethyl bromide and 4.2 g (0.04 mole) of finely powdered sodium carbonate in 50 ml of dry acetone was refluxed for 8.5 hours. After that, the precipitate was filtered off and was washed; 6.4 g of the precipitate was isolated. Acetone was distilled from the filtrate, the residue was washed with sodium carbonate and water and was then extracted with ether. After being dried over calcined sodium sulfate and after a vacuum distillation, there was obtained 4 g of triethyl dithiophosphate (33% calculated on the reacted diethyl S-β-mercaptoethyl dithiophosphate). The product had the following constants:

B.p. 104-105° at 7 mm, $n_D^{20}$ 1.5030, $d_4^{20}$ 1.1146. *

Found %: C 34.02, 33.96; H 7.23, 6.98. $C_6H_{15}O_2PS_2$. Calculated %: C 33.64; H 7.01.

A higher boiling fraction was also isolated during the distillation; this represented the unreacted diethyl S-β-mercaptoethyl dithiophosphate: b.p. 106-109° at 1.5 mm, $n_D^{20}$ 1.5411, $d_4^{20}$ 1.1903.

When the reaction was conducted under these conditions but in the presence of sodium hydroxide, a polymer of ethylene sulfide was isolated from the precipitate which contained sodium bromide. This polymer contained phosphorus and sulfur and was insoluble in organic solvents (alcohol, acetone, ether).

According to its analysis the polymer approximated $(C_2H_5O)_2PSS(CH_2CH_2S)_nPS(OC_2H_5)_2$, where n might be from 18 to 20.

Found %: C 38.39, 39.26; H 6.86, 6.83; P 4.36, 4.36; S 45.36, 45.36.

## SUMMARY

1. The reaction of dialkyl dithiophosphates with ethylene sulfide was studied. It was shown that in this reaction there takes place the addition of dialkyl dithiophosphates to ethylene sulfide with formation of dialkyl S-β-mercaptoethyl dithiophosphates.

2. The presence of β-mercaptogroups in these compounds was proved by their acetylation and alkylation with diazomethane.

## LITERATURE CITED

[1] M. I. Kabachnik, T. A. Mastriukova and V. N. Odnoralova, J. Gen. Chem. 25, 2274 (1955).**

[2] M. Delepine and S. Eschenbrenner, Bull. Soc. Chem. (4), 33, 703 (1923).

[3] E. M. Meade and F. N. Woodward, J. Chem. Soc. 1948, 1894.

[4] G. I. Braz, J. Gen. Chem. 21, 688 (1951).**

[5] R. Oda, C. A. 48, 1935 (1954).

[6] German Patent, 631016 (1936); C.A. 30, 6008 (1936); H. R. Snyder, J. M. Stewart and J. B. Ziegler, J. Am. Chem. Soc. 69, 2672 (1947); H. R. Snyder and E. L. Elice, J. Am. Chem. Soc. 70, 2825 (1948).

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* Constants of triethyl dithiophosphate prepared previously [14]: b. p. 115-115.5° at 10 mm, $n_D^{20}$ 1.5013, $n_4^{20}$ 1.1168.

** Original Russian pagination. See C.B. Translation.

[7] C. C. Culvenor, W. Davies and N. S. Heath, J. Chem. Soc. 1949, 282.

[8] M. Delepine, Compt. rend. 171, 36 (1921); Chem. Zentr. 1920, III, 374.

[9] M. I. Kabachnik, S. T. Ioffe and T. A. Mastriukova, J. Gen. Chem. 25, 684 (1955).*

[10] M. I. Kabachnik, T. A. Mastriukova, M. F. Shostakovskii, E. N. Prilezhaeva, D. M. Paikin, M. P. Shabanova and N. M. Gamper, Doklady Akad. Nauk SSSR 109, 777 (1956);* M. I. Kabachnik, T. A. Mastriukova, Iu. M. Polikarpov, D. M. Paikin, M. P. Shabanova, N. M. Gamper and L. F. Efimova, Doklady Akad. Nauk SSSR 109, 947 (1956).*

[11] L. W. C. Mills and L. N. Owen, J. Chem. Soc. 1952, 817; P. Nylen and A. Olsen, Svensk. Kem. Tidskr. 53, 274 (1941); Chem. Zentr. 1942, I, 604; J. S. Herding and L. N. Owen, J. Chem. Soc. 1954, 1528.

[12] M. I. Kabachnik and T. A. Mastriukova, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1953, 121;* W. E. Bacon and N. M. LeSuer, J. Am. Chem. Soc. 76, 670 (1954).

[13] U.S. Patent 2185660 (1940); C. A. 34, 2865 (1940).

[14] M. I. Kabachnik and T. A. Mastriukova, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1952, 727.*

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Fibers.

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* Original Russian pagination. See C.B. Translation.

# ORGANOPHOSPHORUS INSECTICIDES. SOME DERIVATIVES OF METHYLTHIOPHOSPHONIC AND METHYLDITHIO-PHOSPHONIC ACIDS

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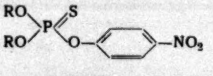
N. M. Gamper and L. F. Efimova

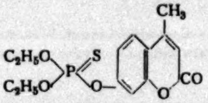
The majority of organophosphorus insecticides are derivatives of thiophosphoric, dithiophosphoric and pyrophosphoric acids [1-3]. In the literature a few insecticides are described which are derivatives of phosphonic and dithiophosphonic acids; among them are esters of methylphosphonic and methylthiophosphonic acids, containing substituted aryl [4], ethylxanthoyl [5] and other [4] groups, as well as the O-ethyl-O-p-nitrophenyl ester of phenylthionophosphonic acid (EPN) [6], which is the only insecticide of the series of thiophosphonic acids which has found a practical application.

In connection with this, it appeared interesting to synthesize a series of derivatives of alkylthio- and alkyldithiophosphonic acids, containing ester groups analogous to those possessed by the known insecticides of the series of thiophosphoric and dithiophosphoric acids and to evaluate their insecticidal action.

We prepared, as the simplest representatives, some derivatives of methylthiophosphonic and methyldithiophosphonic acids which contain atomic groupings analogous to those in Metafos (methyl parathion) (I), Tiofos (parathion) (II), Potasan (III), Karbofos (Malathion) (IV), Metasystox (V) and Merkaptofos (Systox) (VI).



(I) $R=CH_3$,
(II) $R=C_2H_5$.



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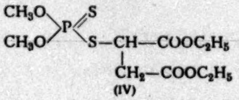

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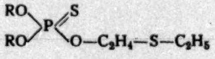


(V) $R=CH_3$,
(VI) $R=C_2H_5$.

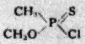
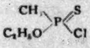
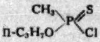
The dichloride of methylthiophosphonic acid, which was prepared by the scheme below, was used as the starting material for the synthesis of these substances. The dichloride of methylphosphonic acid was synthesized by the method of Kinner and Perren [7]:

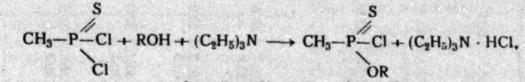
$$CH_3Cl + PCl_3 + AlCl_3 \longrightarrow CH_3PCl_3 \cdot AlCl_4,$$

$$CH_3PCl_3 \cdot AlCl_4 \xrightarrow{H_2O} CH_3POCl_2;$$

then, the oxygen of the phosphoryl group was replaced by sulfur by means of the method developed by us earlier [8]: $5CH_3\underset{\underset{O}{\|}}{P}(O)Cl_2 + P_2S_5 = P_2O_5 + 5CH_3\underset{\underset{S}{\|}}{P}(S)Cl_2$. By the reaction of the dichloride of methylthiophosphonic acid with methyl, ethyl and n-propyl alcohols in the presence of triethyl amine there were synthesized the corresponding chlorides of acid esters of methylthionophosphonic acid (Table 1).

TABLE 1

| Formula | Boiling point (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ |  | Yield (%) | C (%) |  | H (%) |  |
|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  | found | calc. |  | found | calc. | found | calc. |
|  | 54—55° (21) | 1.5085 | 1.2574 | 34.02 | 33.38 | 70 | 16.4,<br>16.5 | 16.6 | 3.9,<br>4.0 | 4.2 |
|  | 55—55.5 (8) | 1.4952 | 1.1992 | 38.17 | 38.00 | 81 | 22.5,<br>22.5 | 22.7 | 4.8,<br>4.9 | 5.1 |
|  | 66—67 (7) | 1.4890 | 1.1549 | 43.13 | 42.62 | 80 | 28.1,<br>27.9 | 27.8 | 6.0,<br>6.0 | 5.9 |



$$CH_3-P(=S)(Cl)-Cl + ROH + (C_2H_5)_3N \longrightarrow CH_3-P(=S)(OR)-Cl + (C_2H_5)_3N \cdot HCl,$$

where R = $CH_3$, $C_2H_5$ and n-$C_3H_7$.

The O-methyl-O-p-nitrophenyl ester of methylthionophosphonic acid (the laboratory number Gd-18) was prepared from the chloride of monomethyl ester of methylthionophosphonic acid and sodium p-nitrophenoxide, while from the acid ethyl ester of methylthionophosphonic acid and sodium p-nitrophenoxide and sodium salt of 4-methyl-7-hydroxycoumarin there were prepared correspondingly the O-ethyl-O-p-nitrophenyl (Gd-5) and O-ethyl-O-7-umbelliferonyl (Gd-19) esters of methylthionophosphonic acid.

The corresponding analogs of Malathion (Gd-27 and Gd-28) were synthesized by the reaction of the indicated acid chlorides with dimethyl and diethyl esters of $\alpha$-mercaptosuccinic acid in the presence of triethylamine.

The chlorides of acid methyl and ethyl esters of methylthionophosphonic acid were also used for the synthesis of substances close in structure to Systox and Metasystox.

O-Methyl-O-$\beta$-methylmercaptoethyl (Gd-39) and O-ethyl-O-$\beta$-ethylmercaptoethyl (Gd-6) esters of methylthionophosphonic acid were prepared by the reaction ofchlorides of the above cited acids with $\beta$-hydroxydiethyl sulfide and $\beta$-hydroxyethyl methyl sulfide, respectively, in the presence of powdered sodium hydroxide.

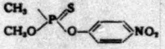
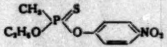
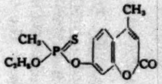
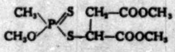
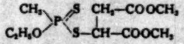
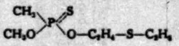
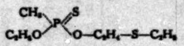
The yields, formulas, constants and analytical data of the synthesized substances are shown in Table 2

## EXPERIMENTAL

Chlorides of acid esters of methylthiophosphonic acid. To 0.1 mole of dichloride of methylthiophosphonic acid [8] in 100 ml of absolute ether there was added, slowly and with cooling by means of water, a mixture of 0.1 mole of anhydrous alcohol and 0.1 mole of triethylamine. Then the reaction mixture was heated on a water bath for 30-40 minutes, after which the precipitated triethylamine hydrochloride was separated and the filtrate distilled in vacuum after the removal of ether. The constants, yields and analytical data for the compound thus prepared are shown in Table 1.

O-Alky-O-p-nitrophophenyl esters of methylthionophosphonic acid (Gd-5 and Gd-18; Table 2). To sodium ethoxide prepared from 0.1 g-atom of sodium and 100 ml of anhydrous alcohol, there was added in small portions a solution of 0.1 mole of p-nitrophenol in 100 ml of dry alcohol, after which the chloride of acid alkyl ester of methylthionophosphonic acid (0.1 mole) was added slowly. The precipitate of sodium chloride was separated, the filtrate was evaporated in vacuum, and the residue crystallized, after chilling with dry ice; it was then recrystallized from petroleum ether.

TABLE 2

| Lab. No. | Formula | Boiling or melting point | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ |  | Yield (in %) | C(%) |  | H(%) |  | P(%) |  | S(%) |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  | found | calc. |  | found | calc. | found | calc. | found | calc. | found | calc. |
| Gd-18 |  | m.p.<br>52—53° | — | — | — | — | 71 | 38.6,<br>38.8 | 38.9 | 4.1,<br>4.0 | 4.1 | 12.4,<br>12.3 | 12.5 | 12.8,<br>12.7 | 12.9 |
| Gd-5 |  | m.p.<br>35—36 | — | — | — | — | 84 | 41.3,<br>41.5 | 41.3 | 4.7,<br>4.7 | 4.6 | 11.6,<br>11.8 | 11.9 | 12.2,<br>12.2 | 12.3 |
| Gd-19 |  | m.p.<br>72—73 | — | — | — | — | 90 | 52.2,<br>52.2 | 52.3 | 5.0,<br>5.1 | 5.1 | 10.2,<br>10.4 | 10.4 | 10.5,<br>10.5 | 10.7 |
| Gd-28 |  | 155—156<br>(3.5 мм) | 1.5269 | 1.2765 | 68.84 | 68.19 | 38 | 33,7,<br>33.7 | 33.6 | 5.3,<br>5.2 | 5.3 | 10.7,<br>10.9 | 10.6 | 22.2,<br>22.3 | 22.4 |
| Gd-27 |  | 166—167<br>(2 мм) | 1.5065 | 1.1818 | 82.64 | 82.04 | 41 | 40.3,<br>40.3 | 40.2 | 6.4,<br>6.4 | 6.3 | 9.4,<br>9.3 | 9.3 | 19.8,<br>19.6 | 19.5 |
| Gd-39 |  | — | 1.5204 | 1.1861 | 51.36 | 51.65 | 59 | 30.2,<br>30.1 | 30.0 | 6.5,<br>6.5 | 6.5 | 14.9,<br>15.0 | 15.3 | 32.3,<br>32.3 | 32.0 |
| Gd-6 |  | 78 (1 мм) | 1.5050 | 1.1124 | 60.84 | 60.79 | 52 | 36.6,<br>36.7 | 36.8 | 7.5,<br>7.7 | 7.6 | 13.9,<br>14.0 | 13.7 | — | — |

O-Ethyl-O-7-umbelliferonyl ester of methylthiophosphonic acid (Gd-19, Table 2). To sodium ethoxide prepared from 0.1 g-atom of sodium and 100 ml of anhydrous alcohol there was added 0.1 mole of 4-methyl-7-hydroxycoumarin, after which 0.1 mole of the chloride of acid ethyl ester of methylthionophosphonic acid was added slowly. Then, the mixture was heated on a steam bath until it attained neutral reaction to litmus The precipitate of sodium chloride was separated and alcohol was distilled in vacuum; the residue crystallized on chilling with dry ice and was twice recrystallized from petroleum ether.

O-Alkyl-S-1,2-dicarbalkoxyethyl esters of methyldithiophosphonic acid (Gd-27 and Gd-28, Table 2). To a mixture of 0.1 mole of the chloride of acid ester of methylthionophosphonic acid and 0.1 mole of triethylamine in 50 ml of absolute ether there was slowly added 0.1 mole of the ester of α-mercaptosuccinic acid, after which the mixture was heated on a water bath for one hour. The precipitated triethylamine hydrochloride was separated, the filtrate was washed with water and dried over sodium sulfate. After the removal of ether, the residue was distilled in vacuum.

O-Akyl-O-β-alkylmercaptoethyl esters of methylthionophosphonic acid (Gd-6 and Gd-39; Table 2). β-Hydroxyethyl alkyl sulfide (0.1 mole) and 0.1 mole of sodium hydroxide were placed in 50 ml of anhydrous benzene. Then, 0.1 mole of the chloride of the acid ester of methylthionophosphonic acid was added slowly. The mixture was heated on a water bath of 60-70° for one hour, after which the precipitate of sodium chloride was separated and benzene was distilled in vacuum; after which the residue was distilled in vacuum (Gd-6) or freed of volatile admixtures by heating to 60° at 2 mm for two hours (Gd-39).

TABLE 3

| Compound | 95-100% kill of insects by emulsion of concentration shown (%) | | Kill of Eurygaster insects (%) on seventh day after infestation /intraplant action of the emulsion |
|---|---|---|---|
| | Pseudococcus maritimus Ehrh. | Eurgygaster integriceps Put. | |
| Gd-18 | 0.015 | 0.005 | — |
| Metafos | — | 0.01 | — |
| Gd-5 | 0.075 | 0.005 | 2.5 |
| Tiofos | > 0.025 | 0.005 | — |
| Gd-19 | 0.10 | 0.05 | — |
| Potasan | 0.015 | — | — |
| Gd-28 | 0.025 | > 0.05 | 5.0 |
| Gd-27 | 0.15 | > 0.05 | 0 |
| Karbofos-1 (Malathion) | — | > 0.01 | — |
| Gd-39 | 0.10 | > 0.05 | 2.5 |
| Gd-6 | > 0.075 | 0.05 | — |

The synthesized compounds were evaluated in laboratory experiments as to insecticidal action of contact and intraplant activity.

Insecticidal properties by contact action were studied on insects of Eurygaster integriceps Put. by the method of immersion into the emulsion with exposure for five seconds and on larvae of advanced age of Pseudococcus maritimus Ehrh. by the method of direct spraying. The toxicity of the compounds was determined on the seventh day according to the concentration of the active principles of the emulsions which caused 95-100% kill of the of the Eurygaster insects and 95-100% dead or paralyzed specimens of the Pseudococcus larvae

The intraplant action of the compounds was examined on the insects of Eurygaster by the technique of preseeding seed treatment of grains of summer wheat. Wheat grains were moistened by 0.6% emulsion of the compounds and were dried in air, being then planted in pots one day later. The Eurygaster insects were deposited onto three-day old sprouts of wheat. The results of the experiment were determined by the mortality of the insects on the seventh day after deposition. As standard substances we used Metafos (I), Tiofos (II), Potasan (III), and Karbofos (Malathion) (IV). The data from the laboratory experiments are in Table 3.

In addition, some of the compounds, specifically Gd-27, Gd-28 and Gd-39 were tested as acaricides with intraplant activity in greenhouse experiments by the spraying technique with Tefranychus sp. on decorative plants; however, the compounds proved to be ineffective.

Among the derivatives of methylthiophosphonic acid only one compound Gd-18 (analog of Metafos) was more toxic in contact action than the corresponding derivative of thiophosphoric acid – Metafos. The other compounds, including Gd-6 (Systox analog), Gd-5 (Tiofos analog) and Gd-19 (Potasan analog) did not show advantages in insecticidal action in comparison with derivatives of thiophosphoric acid.

Substances Gd-27 and Gd-28, which are analogs of Malathion (Karbofos) were characterized by weaker contact insecticidal toxicity against the insects of Eurygaster than Malathion. Against Pseudococcus larvae the substance Gd-27 was a weakly toxic substance, while Gd-28 was equivalent to Tiofos. Both these compounds lacked any intraplant activity.

Thus, the replacement of the alkoxy group in known insecticides from the series of thiophosphoric and dithiophosphoric acids by a methyl group leads to derivatives of methylthiophosphonic and methyldithiophosphonic acids which do possess insecticidal activity. However, only a few of them exceed in insecticidal action the corresponding derivatives of thiophosphoric and dithiophosphoric acids.

## SUMMARY

1. Chlorides of acid esters of methylthionophosphonic acid, containing methoxy, ethoxy and propoxy groups, were prepared from the dichloride of methylthiophosphonic acid.

2. A series of derivatives of methylthiophosphonic and methyldithiophosphonic acids with groupings analogous to those in Tiofos, Metafos, Karbofos, Potasan and Systox were synthesized.

3. The insecticidal properties (contact and intraplant) of the synthesized compounds were studied in laboratory conditions on fall insects of Eurygaster integriceps Put. and on older larvae of Pseudococcus maritimus Ehrh. It was shown that the majority of the prepared compounds are insecticides, which are weaker in activity than are the known insecticides from the series of thiophosphoric and dithiophosphoric acids. Substance Gd-18 (analog of Metafos) exceeds in contact activity the action of Metafos as tested on the insects of Eurygaster integriceps.

## LITERATURE CITED

[1] G. Schrader, Prog. Chem. 22, 712 (1953).

[2] G. Johnson, J. Fletcher, K. Nolan, and J. Cassaday, J. Econ. Entomol. 45, 279 (1952).

[3] G. Schrader, Die Entwicklung neuer Insectizide auf Grundlage von organischen Fluor- und Phosphorverbindungen. Weinheim (1952).

[4] G. Schrader, BIOS, Final report, 1947, No. 714; B. Holmsted, Acta Physiol. Scand. 25, 106 (1951).

[5] U. S. Patent 2668818-2668823; C. A. 49, 5516 (1955).

[6] R. Metcalf and R. March, J. Econ. Entomol. 32, 721 (1949).

[7] A. Kinner and E. Perren, J. Chem. Soc. 1952, 3437.

[8] M. I. Kabachnik and N. N. Godovikov, Doklady Akad. Nauk SSSR 110, 1217 (1956).*

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* Original Russian pagination. See C.B. Translation

# AN INVESTIGATION IN THE FIELD OF ALKANESULFONIC ACIDS

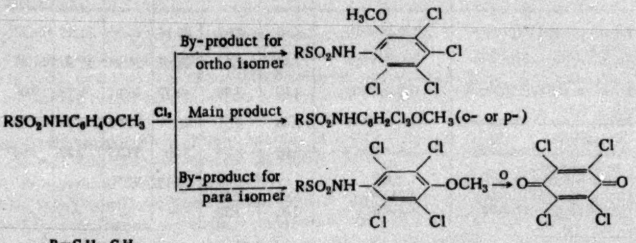
## XVI. CHLORINATION OF ANISIDIDES OF ALKANESULFONIC ACIDS

A. G. Kostsova

We have shown in the previous paper [1] that in the chlorination of anilides of ethane- and butanesulfonic acids there are formed 2,4-dichloro anilides, while in the presence of zinc oxide this reaction leads to still greater yields of these chloro derivatives. The present work had for its purpose the study of the chlorination of o- and p-anisidides of the same sulfonic acids. As a result of the experiments run by us it was shown that the presence of a methoxyl group, as well as its position in the ring, have a notable effect on the character and the yields of the products formed. In addition, the radical of the sulfonic acid (ethyl or butyl) in turn influences (but to a lesser degree) the course of the reaction. Temperature and duration of chlorination have a lesser significance. In chlorination of ethane- and butanesulfoanisidides in the presence of zinc oxide the yields of the resulting compounds are considerably lowered in contrast to the similar chlorination of the unsubstituted anilides.

In chlorination of o-anisidides, dichloroanisidides are formed as the main reaction products, while in the case of derivatives of butanesulfonic acid the yields are lower under otherwise the same conditions. Besides the dichloroanisidides there were isolated in insignificant amounts some tetrachloroanisidides. The reaction products are colorless crystalline substances; the dichloroanisidides are relatively readily soluble in alcohol, while the tetrachloroanisidides are difficultly soluble. This property was used by us for their separation.

In chlorination of p-anisidides it was demonstrated that in the case of ethanesulfoanisidide, dichloro-p-anisidide is formed as the main product, but this occurs with lower yield than for dichloro-o-anisidide; an insignificant amount of tetrachlorobenzoquinone is also formed [2]. In case of butanesulfo-p-anisidide the dichloro derivative was not isolated but the tetrachlorobenzoquinone was isolated in a greater yield than in chlorination of the ethanesulfo-p-anisidide. It seems to us that the formation of this product is the result of a secondary process: evidently at first there is formed the tetrachloroanisidide (as it occurs in chlorination of the o-anisidides), which is then oxidized to tetrachlorobenzoquinone on contact with atmospheric oxygen. The reaction of chlorination of o- and p-anisidides may be expressed by the following general scheme:

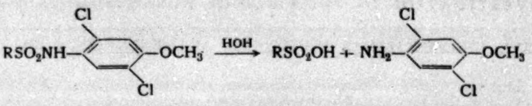


$R = C_2H_5, C_4H_9$

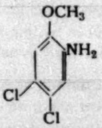
The results described above were obtained in chlorination of the substances with gaseous chlorine which was passed into the reaction mixture at the rate of 3-3.5 ml per second for various time intervals.

We also conducted the chlorination by another method — by mixing solutions of the anisidide and chlorine in in carbon tetrachloride, with the reactants being taken in this case in strictly equimolar amounts. It was shown that in this method of chlorination the same products are formed as in chlorination with gaseous unmetered chlorine, but the yields are lower. Monochloro and trichloro derivatives do not form in either case.

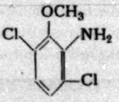
The position of chlorine in the aromatic nucleus of dichloroanisidides was proved by us by the reaction of hydrolysis; in case of dichloro-p-anisidide there was isolated 2,5-dichloroanisidine with m.p. 78-80° (according to literature data, m.p. 79-80°) [3]:



The position of chlorine in dichloro-o-anisidide is not completely clear since the dichloro-o-anisidine, with m.p. 90-92°, which was isolated by us after hydrolysis of the anisidide, is not described in the literature. However, starting from the fact that chlorine is oriented in p-anisidides by both substituents ($RSO_2NH$ and $CH_3O$ groups) as is evident from the indicated equation for the hydrolysis, we suggest that in the case of o-anisidides as there occurs a similar orientation and therefore among all the six possible dichloro-o-anisidines, the one isolated by us has one of the two structures (I) or (II), of which (II) is more probable, since di-



(I)



(II)

chloro-o-anisidides of ethane- and butanesulfonic acids are difficultly soluble in alkali in contrast with all other N-arylamides, which fact may be explained by steric hindrance.

The compounds synthesized by us and the analytical data are in Table 1.

TABLE 1

| Name of compound | Empirical formula | Analytical data (in %) | | | | | |
|---|---|---|---|---|---|---|---|
| | | N | | Cl | | S | |
| | | found | calc. | found | calc. | found | calc. |
| Ethanesulfodichloro-o-anisidide | $C_9H_{11}O_3NSCl_2$ | 4.87 | 4.92 | 25.14 | 24.95 | 11.31 | 11.27 |
| Ethanesulfodichloro-p-anisidide | $C_9H_{11}O_3NSCl_2$ | 4.84 | 4.92 | 24.83 | 24.95 | 11.37 | 11.27 |
| Ethanesulfotetrachloro-o-anisidide | $C_9H_9O_3NSCl_4$ | 4.16 | 3.96 | 40.75 | 40.0 | 9.15 | 9.06 |
| Butanesulfodichloro-o-anisidide | $C_{11}H_{15}O_3NSCl_2$ | 4.46 | 4.51 | 22.85 | 22.93 | 8.28 | 8.35 |
| Butanesulfotetrachloro-o-anisidide | $C_{11}H_{13}O_3NSCl_4$ | 3.68 | 3.77 | 38.0 | 37.27 | 7.20 | 7.08 |
| Tetrachlorobenzoquinone | $C_6O_2Cl_4$ | — | — | 57.17 | 57.72 | — | — |
| Dichloro-o-anisidine | $C_7H_7ONCl_2$ | 6.91 | 7.28 | — | — | — | — |
| Dichloro-p-anisidide | $C_7H_7ONCl_2$ | 7.01 | 7.28 | — | — | — | — |

## EXPERIMENTAL

Chlorination of o-anisidides of ethane- and butanesulfonic acids by means of gaseous chlorine. Into a suspension of 2 g of ethanesulfo-o-anisidide in 10 ml of carbon tetrachloride there was passed a stream of chlorine at the rate of 3-3.5 ml per second for 20 minutes at temperatures of 7° to 16°. Beginning 10-15 minutes after the start of the reaction there separated some small colorless crystals of the dichloroanisidide. The reaction mixture was left until the following day, when the crystals were separated, washed on the filter with carbon tetrachloride and dried. The yield was 1.91 g (74%); after crystallization from alcohol, m.p. 106-108°. From the filtrate left after the separation of the dichloroanisidide there was obtained a viscous oil after distillation of the carbon tetrachloride; this oil was treated with alcohol, whereby a finely crystalline precipitate of the tetrachloroanisidide formed which was separated, washed with alcohol and dried. The yield was 0.03 g (0.94%), m.p. 159-61° (from boiling alcohol). Change of the duration of chlorination from 20 to 60 minutes, as well as of the reaction temperature from 5° to 45° showed little effect on the course of the reaction and on the yields of the products formed. Running the reaction in the presence of zinc oxide lowered the yield of the dichloro products to 15-20%.

The o-anisidide of butanesulfonic acid was chlorinated in the same manner. From 1.5 g of the o-anisidide there was obtained 0.93 g (49%) of dichloro-o-anisidide with m.p. 144-145° (from alcohol).

Dichloro-o-anisidides of ethane- and butanesulfonic acids are readily soluble in benzene, glacial acetic acid, alcohol, carbon tetrachloride and ether which dissolve them on heating, and the substances crystallize out on cooling. The substances are soluble in dilute alkali only on heating and acidification of the alkaline solution leads to precipitation. Tetrachloroanisidides are soluble in alcohol only at the boiling point and are insoluble in alkali.

Chlorination of p-anisidides of ethane- and butanesulfonic acids by means of gaseous chlorine. The chlorination was run analogously to the above example. In case of ethanesulfo-p-anisidide there formed a crystalline dichloro-p-anisidide. The yield from 2 g of p-anisidide was 1.6 g; m.p. 163-165° (from alcohol). After distillation of carbon tetrachloride from the filtrate there remained a viscous yellow oil, from which there was isolated by treatment with boiling alcohol and subsequent cooling, some golden-yellow crystals of tetrachlorobenzoquinone (chloranil), m.p. 290° (from toluene). On mixing hot solutions in alcohol of tetrachlorobenzoquinone and aniline, a quantity of shiny brown crystals of dichlorodianilinobenzoquinone was isolated, which is a characteristic derivative of tetrachlorobenzoquinone [2].

In running the chlorination in the presence of zinc chloride, the yield of dichloroanisidide declines sharply; the same effect is observed in increased volume of the solvent. In chlorination of butanesulfo-p-anisidide the dichloro-p-anisidide was not isolated in a crystalline form. The above-described tetrachlorobenzoquinone, the yield of which in the various experiments ranged from 2.5 to 8.7%, was isolated from the oil formed as the result of distillation of carbon tetrachloride from the reaction mixture, this oil being then boiled with alcohol. The dichloro-p-anisidide of ethanesulfonic acid is soluble in hot benzene, alcohol and glacial acetic acid; it is insoluble in carbon tetrachloride and ether; it is soluble in cold dilute alkali and is precipitated from this solution by acids.

Chlorination of o- and p-anisidides of ethanesulfonic acid by a solution of chlorine. In this case chlorine was used in carbon tetrachloride solution calculated for molar ratios of the anisidide to chlorine equal to 1 : 1, 1 : 2, 1 : 3, and 1 : 4. Into 100 ml of carbon tetrachloride, previously weighed with the vessel, chlorine was added until the desired weight gain was reached, after which a recalculation was made for the content of chlorine per 1 ml of the solution. To a suspension of 2 g of the anisidide in 10 ml of carbon tetrachloride there was added the calculated volume of the chlorine solution. A boiling-up of the mixture and an abundant evolution of hydrogen chloride were observed while the reaction temperature rose to 30°, then slowly dropped to room temperature. In experiments with reactant ratios of 1 : 2, 1 : 3 and 1 : 4 a rapid formation of precipitate was observed, while in the experiment with 1 : 1 ratio no precipitate formed or only a very small one formed, this being, as shown by examination, a mixture of unreacted anisidide and the reaction products. A test for free chlorine with potassium iodide showed that in this experiment the free chlorine is absent after some 10-15 minutes. In remaining experiments the color with potassium iodide is seen even after two hours; in experiments with 1 : 3 and 1 : 4 ratios, some traces of chorine are detectable on the following day. In all cases the precipitates which formed as the result of the reaction were the dichloroanisidide, except for the experiment with 1 : 1 ratio where, as indicated above, a considerable amount of unreacted anisidide was found in the precipitate along with dichloroanisidide. The separated crystals of dichloroanisidide were filtered from the reaction mixture on the following day, carbon tetrachloride was removed from the filtrate, and the residual oil was treated, as described above, and from it there was isolated tetrachloro-o-anisidide (in case of chlorination of o-anisidide - and of tetrachlorobenzoquinone) in case of chlorination of p-anisidide. The results of the chlorination by this technique are summarized in Table 2.

TABLE 2

| Amount of chlorine taken (in g) | Molar ratio of starting materials | o-Anisidide chlorination; amount isolated (in %) | | Isolated in chlorination of p-anisidide (in %) | |
|---|---|---|---|---|---|
| | | dichloro-o-anisidide | tetrachloro-o-anisidide | dichloro-p-anisidide | tetrachlorobenzoquinone |
| 0.66 | 1 : 1 | Mixture of reaction products and starting materials | | | |
| 1.32 | 1 : 2 | 53.7 | 3.0 | 25.0 | — |
| 1.98 | 1 : 3 | 52.2 | 4.2 | 40.1 | 5.2 |
| 2.64 | 1 : 4 | 56.8 | 4.2 | 43.9 | 7.0 |

Thus, chlorination with metered chlorine in solution leads to the same products which are formed in chlorination by unmetered chlorine in gaseous form; the yields of dichloroanisidides however are lower in this case while the yields of the by-products – tetrachloro-o-anisidides and tetrachlorobenzoquinone – are somewhat increased. Chlorination by means of a solution of chlorine was not run with o- and p-anisidides of butanesulfonic acid.

Hydrolysis of dichloroanisidides of ethane- and butanesulfonic acids. The corresponding anisidide (1.5 g) was heated to gentle reflux in 10 ml of dilute sulfuric acid (1 : 1) in a flask with a reflux condenser for several hours until a test sample became completely soluble in water. The mixture, after cooling, was diluted with one volume of water and was then made alkaline. Dichloroanisidine was extracted with ether. After drying with potassium carbonate, the ether was distilled. A viscous brown oil remained as the residue; this oil rapidly crystallized in the case of dichloro-o-anisidide, while in the case of dichloro-p anisidide it crystallized only after a treatment with alcohol, from which the hydrolysis product was precipitated by water.

## SUMMARY

1. The reaction of chlorination of o- and p-anisidides of ethane- and butanesulfonic acids under various conditions was examined.

2. It was shown that under all conditions the main reaction products were dichloroanisidides, while the by-products for o-anisidides were tetrachloro-o-anisidides, and for p-anisidides the by-products consisted of tetrachlorobenzoquinone.

3. It was shown that in the reaction of chlorination of anisidides of alkanesulfonic acids, the alkylsulfonamido and the methoxy groups display an orienting effect in respect to chlorine to an equal degree.

4. It was shown that in hydrolysis of dichloroanisidides the corresponding dichloroanisidines are formed.

## LITERATURE CITED

[1] A. G. Kostsova, N. M. Ianova and Z. N Sushko, J. Gen. Chem. 26, 2855 (1956). *

[2] I. Houben, Methods of Organic Chemistry. III, No. 2, 218 (1935)* *

[3] T. Madesani, Gazz. 62, 402 (1932); C. A. 26, 3802 (1932).

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* * In Russian.

# INVESTIGATIONS IN THE FIELD OF QUINOLINE DERIVATIVES

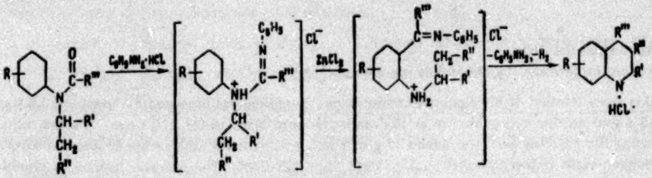
## XIX. A NEW METHOD OF SYNTHESIS OF QUINOLINES BY REARRANGEMENT OF ACYLATED ARYLAMINES*

B. I. Ardashev and V. I. Minkin

Of the various rearrangement reactions of acylated anilines leading to the formation of aromatic aminoketones [1-7] special interest attaches to those rearrangements which ensue in cyclization with the formation of the heterocyclics – acridine [8] and quinoline [9-11]. For this reason the rearrangement of N-ethylacetanilides into quinolines, known in the literature as the Pictet reaction [12], has in recent years been investigated in greater detail [13-15]. It has been found that addition to the starting materials – ethylacetanilide and zinc chloride – of salts of primary or secondary amines not only increases the yield of the quinoline derivatives, but also alters the cyclization mechanism leading to an interesting lepidine rearrangement [15].

In line with the extension of our work on the lepidine rearrangement of ethylacetanilides we have investigated rearrangements of a number of alkylformanilides which proceed in milder conditions in nitrobenzene as the solvent. The experimental data available indicate that the catalytic rearrangements of alkylacylanilides provide a means of preparing various homologs of quinoline and constitute one of a few methods of quinoline synthesis of a general character.

The mechanism of the rearrangement investigated differs from that of the Pictet reaction and does not involve the splitting off of an alkyl radical from the nitrogen atom, since α, β-dimethylindole, the formation of which might be expected in the latter case [13], does not form lepidine on interacting with aniline hydrochloride. As a result of investigations carried out it was established that the first stage of the reaction is the formation of N,N'-diaryl-N-alkyl-acylamidine which is obtained by heating amine salts with their acyl derivatives to a temperature of 150-160° [16, 17]. In point of fact, improved yields were obtained by using equivalent amounts of the amine salts; addition of salts of tertiary amines, which are incapable of yielding amidines, gave low yields of the final product of the rearrangement amounting to only 1-2% [4]. At elevated temperature, amidines rearrange into the anil of the corresponding o-aminocarbonyl compound which then undergoes cyclization into quinoline.



$R = H, CH_3, OCH_3$
$R', R'', R''' = H, CH_3$

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* Communication XVIII, see [15].

The possibility of such a rearrangement is confirmed, firstly, by the formation of p-aminobenzaldehyde and p-aminoacetophenone on introducing aniline into the Goesch synthesis [18] with nitriles, in which case the intermediate product of the reaction is, evidently, N-phenylacylamidine which undergoes further isomerization [19]; a further confirmation is provided by our synthesis of quinoline from N-ethyl-N,N'-diphenylformamidine hydrochloride. Amidines possess a tendency to undergo rearrangements [20].

On the basis of the amidine rearrangement it is now possible to elucidate the hitherto obscure mechanism of the formation of flavaniline from acetanilide hydrochloride [21], of aminoacetophenones from acetanilide, in which case the presence of diphenylacetyamidine was detected among the reaction products [1], and of some other reactions.

## EXPERIMENTAL

Preparation of starting materials. The starting alkylformanilides were prepared by the following methods: (a) by alkylation of formanilides with alkyl bromides in the presence of alcoholic KOH [22]; (b) by alkylation through the N-formyl-sodium derivatives of amines [23-25]; (c) by formylation of ethylanilines [26] in toluene [27]. The acetyl derivatives were prepared by interacting ethylanilines with acetic anhydride.

Preparation of quinoline derivatives. The rearrangement of the acetanilides was carried out by the method described earlier [15]; rearrangement of formanilides was effected by the following general method. The alkylformanilide (1 mole) was mixed with aniline hydrochloride (1 mole) and zinc chloride (1.1-1.4 mole) and the mixture was diluted with 5-6 times its weight of nitrobenzene and refluxed for 2-3 hours. The nitrobenzene was removed from the acid solution by steam-distillation, after which the bases were distilled from alkaline solution; tertiary amines were purified with phthalic anhydride [28] and subsequently distilled. The picrates were recrystallized from ethanolacetone solution, and after 1-2 recrystallizations had the required melting points. Only in the case of 6-methylquinoline was it necessary to purify the picrate through two cycles of the Manske treatment [29]. The results are listed in the Table.

| Alkylacylanilide | Quinoline derivative (position and substituent | Boiling point | Yield (in %) | Melting point of picrate |
|---|---|---|---|---|
| Ethylformanilide | Quinoline | 230—240° | 11 | 198° |
| Isopropylformanilide | 2-Methyl | • | 4 | 188—189 |
| n-Propylformanilide | 3-Methyl | • | 5 | 185 |
| Ethylacetanilide [15] | 4-Methyl | 235—265 | 17 | 211—212 |
| Ethylform-p-toluidide | 6-Methyl | 240—257 | 15 | 224 |
| Ethylform-o-toluidide | 8-Methyl | 226—250 | 9 | 196 |
| Ethylacet-p-toluidide [15] | 4,6-Dimethyl | 235—270 | 20 | 237 |
| Ethylacet-o-toluidide | 4,8-Dimethyl | 93—100 (5 мм) | 14 | 214—215 |
| Ethylform-m-xylidide | 6,8-Dimethyl | 90—106 (5 мм) | 12 | 226—227 |
| Ethylacet-m-xylidide | 4,6,8-Trimethyl | • | 6 | 206 |
| Isopropylform-m-xylidide | 2,6,8-Trimethyl | 250—270 | 5 | 184—186 |
| Ethylform-p-anisidide | 6-Methoxy | 240—265 | 18 | 209 |
| Methylacet-p-anisidide•• | 6-Methoxy | • | 2 | 205 |

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• Isolated as the picrate.

•• Reaction proceeds by the indole mechanism [13].

Quinoline from N-ethyl-N,N'-diphenylformamidine. Amidine was prepared by heating 17.5 g of formethylaniline and 15.4 g of aniline hydrochloride at 150° under reduced pressure for $1\frac{1}{2}$ hours. To the semi-solid mass, constituting the amidine salt, was added 17 g of $ZnCl_2$ and 85 ml of nitrobenzene and the mixture was refluxed for 2 hours. Yield of the quinoline, 1.5 g (10%), b.p. 225-240°. The picrate, formed in alcohol, melts at 191°, and after recrystallization from acetone, at 199°. Mixture of this picrate with an authentic sample did not depress the melting point; the same applies to all other quinolines listed in the Table.

The following compounds have not so far been described in the literature: ethylform-o-toluidide (b.p. 255-265°), ethylform-p-toluidide (b.p. 142°, 4 mm), ethylform-m-xylidide (b.p. 265-270°), ethylacet-m-xylidide (b.p. 265°), ethylform-p-anisidide (b.p. 160-175°, 7 mm), isopropylform-m-xylidide (b.p. 260-275°) and N-ethyl-N,N'-diphenylformamidine hydrochloride (m.p. 150-154°).

## SUMMARY

1. The rearrangement of a number of alkylacylanilides in the presence of aniline hydrochloride has been investigated.

2. The general nature of this reaction and its use in the synthesis of various quinoline derivatives has been demonstrated.

3. It has been established that the mechanism of the reaction involves the formation of N-alkyl-N,N'-diarylamidines as intermediate products.

4. The reaction investigated is an entirely novel method of synthesis of quinoline derivatives.

## LITERATURE CITED

[1] F. Meyer and A. Hofmann, Monatsch., 36, 707 (1915).

[2] German Patent 56971; Fridl., 3, 21.

[3] F. D. Chattaway, J. Chem. Soc., 1, 1904, 386.

[4] A. W. Chapmann, J. Chem. Soc., 1925, 127; Zbl., 1926, I, 2089.

[5] E. Meitzner, J. Am. Chem. Soc., 57, 2327 (1935).

[6] D. N. Kursanov, J. Gen. Chem., 13, 286 (1943).

[7] B. I. Ardashev and V. I. Minkin, Ibid, 27, 1261 (1957).*

[8] A. Bernthsen, Lieb. Ann., 224, 1 (1884).

[9] E. Besthorn and O. Fischer, Ber., 16, 68 (1883).

[10] A. Pictet and R. Bunzl, Ber., 22, 1847 (1889).

[11] A. Pictet and J. Fert, Ber., 23, 1903 (1890).

[12] B. I. Ardashev, Usp. Khim., 23, 45 (1945).

[13] B. I. Ardashev and B. A. Tertov, J. Gen. Chem., 22, 2200 (1952).*

[14] D. Klamann, Monatsch., 84, 925 (1953).

[15] B. I Ardashev, Proc. Acad. Sci. USSR, 110, 783 (1956).*

[16] G. Tobias, Ber., 15, 2449 (1882).

[17] C. C. Price, and R. M. Roberts, J. Am. Chem. Soc., 68, 1255 (1946).

[18] Organic Reactions, Vol. 5, 284 (1951). **

[19] Wu-Hao-Tsing, J. Am. Chem. Soc., 66, 69 (1944).

[20] O. A. Reutov, Theoretical Problems of Organic Chemistry, Moscow State Univ. Press., 394 (1956).**

[21] O. Wallach, Ber., 15, 208 (1882).

[22] A. Pictet and P. Crepieux, Ber., 21, 1109 (1888).

[23] V. Higginbottom, Reactions of Organic Compounds, Moscow, United Sci.-Tech. Press, 350 (1939).***

[24] L. Houben, Methods of Organic Chemistry, Vol. IV, State Chem. Press (1949).***

[25] J. Nomura, C. A., 48, 11371 (1954).

[26] K. Weygand, Experimental Methods in Organic Chemistry, Vol. II, Foreign, Press, 251 (1952).***

---

*Original Russian pagination. See C.B. Translation.

** In Russian.

***Transliteration of Russian – Publisher's note.

[27] Organic Syntheses, Vol. 3, 320.**

[28] B. A. Porai-Koshits,* Author's Cert. No. 47297 (1935).

[29] R. H. F. Manske, L. Marion, and F. Leger, J. Can. Res., 20B, 133 (1942).

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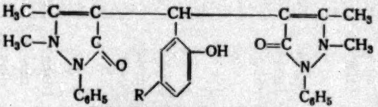
*In Russian.

# INTERACTION OF AQUEOUS SOLUTIONS OF SALTS OF TETRAVALENT TITANIUM WITH PYRAZOLONE DERIVATIVES

R. G. Beiles*

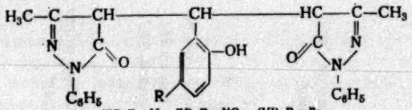
Earlier we have established that during the interaction of aqueous solutions of salts of $Ti^{4+}$ with diantipyryl-o-hydroxyphenylmethane (I) there appears an orange-yellow coloration, or else there are formed precipitates of unknown composition [1].



(I) R=H, (II) R=$NO_2$, (III) R=Br.

It has now been found that not only compound (I), but also some other products of the interaction of salicylaldehyde with pyrazolone derivatives react readily with titanic ions; the reaction products may be obtained in the form of well-defined crystalline compounds. Below are described results of an investigation of the interaction of titanium ions with bis-pyrazolone derivatives of salicylaldehyde.

1. Interaction of $Ti^{4+}$ ions with dipyrazolonyl-o-hydroxyphenylmethane and its derivatives. (a) Interaction in the presence of weakly basic compounds. If a solution of $CH_3COONa$, $K_2CO_3$, urotropine or of some other weakly-basic compound is added to an acid aqueous-alcoholic solution containing $TiCl_4$ and dipyrazolonyl-o-hydroxyphenylmethane (IV), there is formed an orange-colored precipitate (Fig. 1). Precipitation takes place at a pH of 3 to 5.



(IV) R=H, (V) R=$NO_2$, (VI) R=Br.

An interesting property of this substance is its exceptional stability, characteristic of titanium derivatives, towards the action of NaOH, KOH and other alkalis. The compound is also stable towards the action of concentrated phosphoric acid.

Analysis has shown that one atom of Ti is combined with two molecules of compound IV; the composition of the substance may be represented by the formula 2 DipTi=O, where Dip represents dipyrazolonyl-o-hydroxyphenylmethane.

In a similar manner were obtained titanium derivatives containing a nitro group (from compound V) and a bromine atom (from compound VI) in the benzene nucleus.

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* With the collaboration of N. G. Trotsenko, M. A. Timchenko, A. L. Russkii, and Iazova, all students at the Upper-Altai Teachers' Training Institute.

Compounds Formed as a Result of Interaction of bis-Pyrazolone Derivatives with $Ti^{4+}$ Ions in Aqueous-Alcoholic Solutions (The table gives the color of the substance, microscopic appearance of the crystals and the decomposition temperature*)

| Starting bis-pyrazolone derivatives | Reaction conditions | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Result on addition of weak-base | Result on addition of inorganic salts | | | | | | | |
| | | KCl | KI | $KNO_3$ | $KClO_3$ | $NH_4ClO_4$ | KCNS | $K_2SO_4$ | $K_2S_2O_8$ |
| (IV) | Red, rectang. prisms and rombi, 265° | Red, cubes, 275° | Red, cubes and octahedrons, 220° | Orange prisms 240° | Orange, cubes, 130° | Orange, cubes and prisms, 210° | Red, fine cubes, 250° | Organge, prisms, 230° | Red, prisms and cubes, 250° |
| (V) | Orange, prisms, decomposes above 350° | Orange, prisms, 250° | Red, prisms, and plates, 230° | Orange, prisms, 215° | Orange, prisms, 300° | Orange, rombi and plates, 240° | Red, prisms and plates, 210° | Orange, fine prisms, decomp. above 350° | Orange, prisms and plates, decomp. above 350° |
| (VI) | Red, X-shaped dendrites, 295° | Yellow, needle clusters and prisms, 290° | Red, prisms and cubes, 300° | Orange, prisms, 315° | Orange prisms, 285° | Yellow, 270° | Red prisms and cubes, 265° | Orange, fine prisms, decomp. above 350° | Orange, prisms, decomp. above 360° |
| (I) | No reaction | Orange, prisms, 240° | Red, needle clusters, 270° | Orange, needles, 285° | Orange, needle clusters, 230° | Orange, fine needles, 280° | Red, needle clusters, 220° | — | — |
| (II) | No reaction | — | Orange, needles or prisms, 240° | Yellow, needle clusters, 260° | Yellow, needle clusters, 230° | Orange, needles or prisms, 260° | Red, needles or prisms, 230° | — | — |
| (III) | No reaction | | Red, needle clusters, 280° | Orange, needle clusters, 290° | Orange, prisms, 260° | Orange, prisms, 280° | Red, prisms, 230° | — | — |
| | | Compounds 2DTI=O | Compounds $2DTiX_2$ | | | | | | |

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* Fusion and decomposition comes about gradually; the table gives the temperature at which a noticeable change begins.

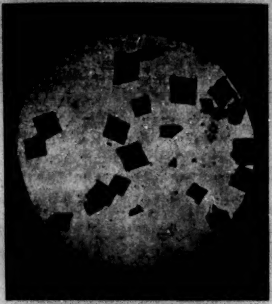


Fig. 1. Crystals of the compound 2 Dip Ti=O (x 140).

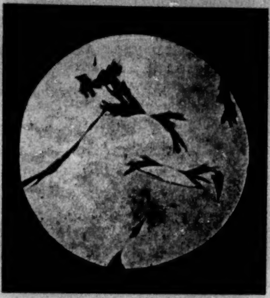


Fig. 2. Crystals of the compound 2 Diant $Ti(NO_3)_2$. (x 140).

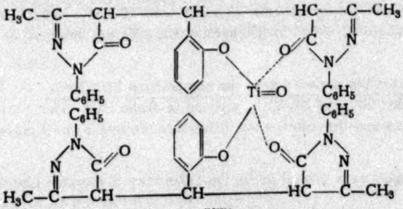
(b) Interaction of $Ti^{4+}$ ions with dipyrazolonyl-o-hydroxyphenylmethane in the presence of various salts. Crystalline precipitates may also be obtained from solutions containing $Ti^{4+}$ and dipyrazolonyl-o-hydroxyphenylmethane even in the absence of weak bases; namely, on addition of salts of the most anions (X). Analyses have shown that the composition of the precipitates may be expressed by the formula 2 Dip $TiX_2$. Our investigations included precipitates in which X was Cl, I, $NO_3$, $ClO_3$, $ClO_4$, CNS, $S_2O_8$, as well as some other anions (see Table). The compounds resemble in many respects those described above. Analogous titanium derivatives containing a nitro group (from compound V) and a bromine atom (from compound VI) have also been prepared.

Thus, dipyrazolonyl-o-hydroxyphenylmethane and its derivatives form two series of compounds with tetravalent titanium represented, respectively, by the formulas 2 Dip Ti=O and 2 Dip $TiX_2$.

2. Interaction of $Ti^{4+}$ ions with diantipyryl-o-hydroxyphenylmethane and its derivatives. Diantipyryl-o-hydroxyphenylmethane (I) and its nitro and bromo derivatives (II and III) react with $Ti^{4+}$ in the presence of various salts in a manner similar to the reaction of these ions with dipyrazolonyl-o-hydroxyphenylmethane (see par. 16) giving crystalline precipitates of the composition 2 Diant $TiX_2$ (see Fig. 2). This reaction was used by us in a quantitative estimation of titanium [2].

The precipitates are decomposed gradually, over a period of several hours, by solutions of alkali, with the formation of titanium hydroxide. The derivative in which X = I, reacts only very slowly with $AgNO_3$ solution.

In contrast to dipyrazolonyl-o-hydroxyphenylmethane (IV), compounds I to III do not form derivatives of the type which might be represented by 2 Diant Ti=O, i.e. the reaction does not proceed in the presence of weak bases. This difference in behavior is apparently due to the presence in compound (IV) of a labile hydrogen atom owing to which the compound exhibits amphoteric properties; the compound dissolves in alkalis with the formation of its enolic form [3]. By contrast, compound (I) does not undergo a similar tautomeric transformation.



(VII)*

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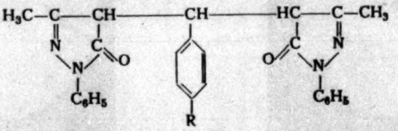
*In the central portion of this formula the group Ti = 0 may also be replaced by $TiX_2$.

The properties of the compounds obtained and, in particular, their stability towards the action of alkalis indicate that the titanium atom is linked by complex-type bonds to the molecules of bis-pyrazolone compounds. In view of this, these compounds may be represented by the structural formula (VII) [in the case of those derived from compound (IV)].

The formulas proposed may be comfirmed to some extent by the following facts. If the OH group in the benzene ring is absent [as in dipyrazolonyl-phenylmethane (VIII) or diantipyrylphenylmethane], the reaction with titanium does not occur.



(VIII) R=H; (IX) R=OH.

No reaction will take place, either, if the OH group is in the para-position [dipyrazolonyl-p-hydroxyphenylmethane (IX) and diantipyryl-p-hydroxyphenylmethane]. Consequently, the presence of the hydroxy group in the ortho-position is a prerequisite for reaction with titanium. However, the data available are still insufficient in order to establish definitely the structure of these compounds.

## EXPERIMENTAL

1. Preparation of bis-pyrazolone derivatives. Compounds (I-VI, VIII-IX) were prepared by the method described earlier for diantipyryl-o-hydroxyphenylmethane [1] with certain modifications in each case. The separations into "white" and "yellow" isomers [3] were not carried out.

Diantipyryl-2-hydroxy-5-nitrophenylmethane (II) was obtained from antipyrine and 5-nitrosalicylaldehyde as a white substance melting at 268-270° (for the free base).

Found %: C 65.94; H 5.06; N 13.06; $C_{29}H_{27}O_5N_5$. Calculated %: C 66.29; H 5.18; N 13.33.*

Diantipyryl-2-hydroxy-5-bromophenylmethane (III) was prepared from antipyrine and 5-bromosalicylaldehyde; white substance melting at 269-271°. The hydrochloride melts at 149-150°

Found %: N 9.89; Br 14.01. $C_{29}H_{27}O_3N_4Br$. Calculated %: N 10.01; Br 14.28.

Diantipyryl-p-hydroxyphenylmethane was prepared from antipyrine and p-hydroxybenzaldehyde [1].

Dipyrazolonyl-2-hydroxy-5-nitrophenylmethane (V) was obtained from 1-phenyl-3-methylpyrazolone-5 and 5-nitrosalicylaldehyde as a yellow to orange substance, m.p. 220-222°.

Found %: C 64.86; H 4.38; N 14.04. $C_{27}H_{23}O_5N_5$. Calculated %: C 65.18; H 4.66; N 14.07.

Dipyrazolonyl-2-hydroxy-5-bromophenylmethane (VI) was obtained from 1-phenyl-3-methylpyrazolone-5 and 5-bromosalicylaldehyde. Light yellow substance, m.p. 228-230°.

Found %: N 10.41; Br 14.76. $C_{27}H_{23}O_3N_4Br$. Calculated %: N 10.55; Br 15.04.

Dipyrazolonyl-p-hydroxyphenylmethane (IX), m.p. 159-160° [3]; dipyrazolonylphenylmethane (VIII), m.p. 227-229° [4]; dipyrazolonyl-o-hydroxyphenylmethane (IV) was obtained as a yellowish-white substance melting at 220-222° [3].

2. Preparation of titanium derivatives of the composition 2DipTi=O. To 200 ml of 2% alcoholic solution of compound (IV) was added 20 ml of 1% $TiCl_4$ solution in dilute HCl. The mixture developed an orange-red coloration. Whenever necessary the solution was filtered to remove a small amount of a precipitate and to the

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* Determinations of nitrogen were carried out in the Laboratory of Organic Chemistry of the Ural Polytechnical Institute.

filtrate was added a 10% aqueous solution of urotropine until a copious yellow precipitate formed. In place of urotropine, solutions of $CH_3COONa$, $K_2CO_3$, potassium citrate and other weakly-basic substances may be used. The mixture was heated to reflux; on cooling the yellow precipitate changed in color to an orange-red. After washing with water, alcohol and ether there was obtained 3.0 g of the titanium derivative (for microscopic view of the crystals see Fig. 1).

The substance is sparingly soluble in alcohol and acetone, slightly more soluble in dioxane and pyridine. In dilute and concentrated solutions of NaOH and KOH it forms orange-colored solutions which are stable in the cold; on acidifying these alkaline solutions the compound precipitates unchanged. On boiling the alkaline solution there occurs hydrolysis with the formation of $TiO_2$ and dipyrazolonyl-o-hydroxyphenylmethane. Solution of the compound in $NH_4OH$ is unaffected on boiling. Above 265° the compound decrepitates with decomposition.

Found %: C 66.75; H 4.64; N 11.13; Ti 5.07. $C_{54}H_{46}O_7N_8Ti$. Calculated %: C 67.07; H 4.80; N 11.58; Ti 4.95.

The titanium derivatives of compounds (V) and (VI) were obtained in a manner similar to that described above (see Table).

3. Preparation of titanium derivatives of the composition $2DTiX_2$. From compounds (I-VI) and $TiCl_4$ were obtained aqueous-alcohol solutions of the titanium derivatives, as described in section 2 above. To the reaction mixture was added a 5-10% solution of KI, $KNO_3$ or of some other salt, depending on the nature of the radical X to be introduced into the molecule.* Addition of certain salts for example, of $K_2S_2O_8$, induces a distinct crystallization process in the cold. The derivatives of dipyrazolonyl-o-hydroxyphenylmethane and of its analogs (IV-VI) resemble in their properties the products of the type 2DipTi=O described above.

Derivatives of diantipyryl-o-hydroxphenylmethane (I-III) differ from the other derivatives in their lower stability towards alkalis (slow hydrolysis in the cold) as well as in their considerably lower solubility and good crystallizing properties, particularly in the case $NO_3$ and $ClO_3$ derivatives [2].

The results of the analysis of the derivative obtained from diantipyryl-o-hydroxyphenylmethane (I), with X = I, are given below as an example:

Found %: N 8.73; 20.04; Ti 3.85. $C_{58}H_{54}O_6N_8I_2Ti$. Calculated %: N 8.89; I 20.13; Ti 3.80.

The compounds prepared are listed in the Table.

## SUMMARY

Interaction of aqueous solutions of salts of tetravalent titanium with bis-pyrazolone derivatives of salicylaldehyde (D) gives rise to the formation of compounds having the composition 2 DTi=O and 2 $DTiX_2$, where X = Cl, I, $NO_3$ and other radicals. 40 compounds of both types have been prepared and a few hitherto unknown bis-pyrazolone derivatives have been described.

## LITERATURE CITED

[1] S. I. Gusev and R. G. Beiles, Proc. of the Commission on Anal. Chem., 5 (8), 68 (1954).

[2] R. G. Beiles, Factory Labs, 22, 1296 (1956).

[3] A.E. Porai-Koshits, B. A. Porai-Koshits, and N. G. Lipnd, J. Gen. Chem. 26, 872 (1956).

[4] Stolz, Ber. 28, 631 (1895)

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* Compounds in which X = Cl may be precipitated from the solution by the addition of water, or they may be obtained by evaporating the solution without the addition of any reagents.

# ANILIDES OF ALKYLSULFONAMIDOPHOSPHORIC ACIDS

A. V. Kirsanov and N. L. Egorova

The action of aniline on trichlorophosphazosulfonalkyls [1] might be expected to give anilidodichlorophosphazosulfonalkyls of the type $RSO_2N=PCl_2(NHC_6H_5)$ (I), dianilidochlorophosphazosulfonalkyls of the type $RSO_2N=$ $=PCl(NHC_6H_5)_2$ (II), and trianilidophosphazosulfonalkyls of the type $RSO_2N=P(NHC_6H_5)_3$. But type (I) substances were not obtained (Cf. [2]). Even with a large excess of the trichlorophosphazosulfonalkyl it was impossible to isolate any of (I) from the reaction products. Dianilidochlorophosphazosulfonalkyls (II) were obtained in satisfactory yields by the reaction of trichlorophosphazosulfonalkyls with aniline in carbon tetrachloride solution. These were found to be colorless crystalline substances of neutral character, easily hydrolyzed to dianilides of alkylsulfonamidophosphoric acids (III), by heating their solution in 96% alcohol, or by boiling with water, according to the equation

$$RSO_2N{=}PCl(NHC_6H_5)_2 + H_2O \rightarrow HCl + \underset{(III)}{RSO_2NHPO(NHC_6H_5)_2}$$

Readily soluble salts of III were formed by the action of aqueous solutions of caustic alkalis and ammonia on II. Free III was precipitated on acidification of a solution of the salt; for this reason it was not necessary to isolate II in the preparation of III – it was sufficient to treat the reaction mixture with sodium hydroxide solution, and subsequently isolate III.

III salts were found to be colorless crystalline substances, with a very bitter taste, and were not hydrolyzed even by prolonged boiling with water or alkali solutions. They were slowly hydrolyzed on heating with dilute mineral acids to form the amides ofalkylsulfonic acids and the anilides of phosphoric acid. They were fairly strong monobasic acids.

The trianilidophophazosulfonalkyls (IV) were obtained in good yield by the prolonged heating of trichlorophosphazosulfonalkyls with excess of aniline in benzene solution. They were found to be colorless crystalline substances, with a bitter taste, of a neutral character and very resistant to the action of alkali (cf. [3]). They remained unchanged even after prolonged boiling with alcoholic alkali. The other properties of substances II to IV are given in the experimental part.

## EXPERIMENTAL

Dianilidochlorophosphazosulfonethyl (V). A solution of 0.05 mole of freshly distilled aniline in 15.0 ml of $CCl_4$ was added slowly, with vigorous stirring, to a solution of 0.01 mole of trichlorophosphazosulfonethyl in 15.0 ml of dry $CCl_4$. The reaction was accompanied by the liberation of a large amount of heat; so the reaction mixture was cooled by water and ice, to maintain the temperature between 5 and 15°. If the reaction was carried out at a higher temperature, a considerable quantity of trianilidophosphazosulfonethyl was formed, and the yield of V was reduced. The reaction mixture was allowed to stand for two days at room temperature, after which the mixture of V and aniline hydrochloride was filtered off under suction, and the V was extracted with boiling benzene. The V crystallized out from the cold benzene solution in the form of agglomerates of transparent prisms. Yield 60.2%, m.p. 88-89°.

Found %: N 11.59; equiv. after hydrolysis, 1.99, 1.97. $C_{14}H_{17}O_2N_3SPCl$. Calculated %: N 11.78. equiv. after hydrolysis, 1.00, V was readily soluble in acetone and dioxane, and readily soluble on heating in benzene, ether, petroleum ether, carbon tetrachloride and ethyl acetate.

Dianilidochlorophosphazosulfon-n-butyl (VI) was readily soluble in $CCl_4$. After carrying out the reaction and filtering off the aniline hydrochloride, the filtrate was evaporated on a water bath under reduced pressure, and the residue was washed with a small amount of cold benzene to remove excess aniline, and recrystallized from boiling benzene, if necessary with the addition of active carbon. VI consisted of fine prisms, m.p. 176-178°, yield 65.3%.

Found %: N 11.15. $C_{16}H_{21}O_2N_3SPCl$. Calculated %: N 10.90.

VI was readily soluble in acetone, dioxane and carbon tetrachloride, and with considerable difficulty in benzene, ether, petroleum ether, and ethyl acetate. V and VI gave VII and VIII (see below) on heating with alcohol, or by the action of caustic alkali solutions.

Dianilide of ethylsulfonamidophosphoric acid (VII). A mixture of 0.01 mole of V and 40.0 ml of N aqueous caustic soda was heated to boiling and filtered, and the hot solution was treated with 5N hydrochloric acid until acid to congo red. The crystalline hydrate of VII then precipitated in the form of fine colorless prisms Yield 62.2%, m.p. 127-130°.

Found %: $H_2O$ 2.59. $(C_{14}H_{18}O_3N_3SP)_2 \cdot H_2O$. Calculated %: $H_2O$ 2.58.

The crystalline hydrate was completely freed from water by heating to 100°, or by recrystallization from benzene. Anhydrous VII crystallized from benzene in the form of fine needles, m.p. 158-160°.

Found %: N 12.49. Equiv. 1.006, 0.993. $C_{14}H_{18}O_3N_3SP$. Calculated %: N 12.39. Equiv. 1.000.

Dianilide of n-butylsulfonamidophosphoric acid (VIII). This was obtained in the same way as VII. Yield 59.9%, m.p. 188-89°. Fine thin prisms (from water).

Found %: N 11.33, 11.23. Equiv. 0.99, 1.010. $C_{16}H_{22}O_3N_3SP$. Calculated %: N 11.44. Equiv. 1.000.

VII and VIII had a very bitter taste. They were readily soluble in acetone, dioxane, alcohol and ethyl acetate and they were soluble in hot water and benzene, and with great difficulty in $CCl_4$ and petroleum ether. VII and VIII could be obtained without the isolation of V and VI in the pure state. To do this, the crude intermediates were treated with a hot solution of caustic soda, the solution was decolorized with active carbon, and VII and VIII were precipitated with hydrochloric acid.

Trianilidophosphazosulfonethyl (IX). A solution of 0.01 mole of trichlorophosphazosulfonethyl in 10.0 ml of dry benzene was added to a solution of 0.08 mole of freshly distilled aniline in 10.0 ml of benzene, with stirring and cooling (much heat was liberated). The reaction mixture was then boiled under reflux on a water bath for 10 hours. The precipitated mixture of IX and aniline hydrochloride was filtered under suction, and washed with benzene, a few times with water, with N hydrochloric acid, with 0.5 N sodium hydroxide (to remove VII) and again with water. Yield 79.0%, m.p. 251-252°, crystallized from alcohol as long needles.

Found %: N 13.66. $C_{29}H_{23}O_2N_4SP$. Calculated %: N 13.53.

Trianilidophosphazosulfon-n-butyl (X). This was obtained in the same way as IX. Yield 78.6%, m.p. 232-233°; crystallized from benzene or alcohol in the form of small needles.

Found %: 12.44. $C_{22}H_{27}O_2N_4SP$. Calculated %: N 12.66.

IX and X had a bitter taste, and were insoluble in water or aqueous solutions of caustic alkali or acid. They dissolved on heating in acetone, dioxane, alcohol and ethyl acetate, but were insoluble in $CCl_4$ and petroleum ether.

## SUMMARY

Dianilidochlorophosphazosulfonalkyls, trianilidophosphazosulfonalkyls and dianilides of alkylsulfonamidophosphoric acids have been prepared and their properties have been described.

## LITERATURE CITED

[1] A. V. Kirsanov and N. L. Egorova, J. Gen. Chem. 25, 187 (1955).*

[2] A. V. Kirsanov and E. A. Abrazhanova, J. Gen. Chem., Coll. II, 1059, 1370 (1953).

[3] A. V. Kirsanov and V. I. Shevchenko, J. Gen. Chem. 24, 474, 882, 1980 (1954).*

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*Original Russian pagination. See C.B. Translation.

# SALTS OF THE ACID FLUORIDES OF ARYLSULFONAMIDO-PHOSPHORIC ACIDS

A. V. Kirsanov and E. S. Levchenko

The readily available and sufficiently studied trichlorophosphazosulfonaryls [1] and the products of their hydrolysis, the acid dichlorides of arylsulfonamidophosphoric acids [2], are very reactive compounds and can be used as starting materials for the synthesis of various new organic phosphorus compounds [3]. Considerable interest attaches to the investigation of fluorine compounds analogous to the trichlorophosphazosulfonaryls and to the acid dichlorides of arylsulfonamidophosphoric acids. Attempts to replace chlorine by fluorine in the latter, using sodium or potassium fluorides in neutral organic solvents, did not meet with success. Antimony trifluoride was also found to be unsuitable for this purpose, as it was impossible to isolate the individual products from the reaction mixture.

It is known that chlorine is readily replaced by fluorine in various acids in reactions with aqueous solutions of potassium fluoride or bifluoride; for example, the acid dichlorides of the diethylamides of phosphoric and thiophosphoric acids, when heated with a saturated aqueous solution of potassium fluoride, give the corresponding acid fluorides [4]. Heat was liberated when trichlorophosphazosulfonaryls reacted with a saturated aqueous solution of potassium fluoride. In this reaction, besides the replacement of chlorine atoms by fluorine, there was partial hydrolysis leading to the formation of potassium salts of the acid difluorides of arylsulfonamidophosphoric acids, according to the over-all scheme:

$$AsSO_2N{=}PCl_3 + 6KF + H_2O \rightarrow K^+(ArSO_2NPOF_2)^- + 3KCl + 2KHF_2$$

The same compounds were obtained by the interaction of the acid dichlorides of arylsulfonamidophosphoric acids with an aqueous solution of potassium fluoride, according to the over-all scheme:

$$ArSO_2NHPOCl_2 + 4KF \rightarrow K^+(ArSO_2NPOF_2)^- + 2KCl + KHF_2$$

In this case the reaction was less vigorous, and it was necessary to heat the reaction mixture to 30-40°.

The reaction of the formation of the potassium salts of the acid difluorides of arylsulfonamidophosphoric acids passed through the stage of the potassium salts of the acid dichlorides of the arylsulfonamidophosphoric acids, $ArSO_2NKPOCl_2$ [5], which then exchanged chlorine for fluorine. This was shown by the interaction of the acid dichloride of phenylsulfonamidophosphoric acid with potassium fluoride solution at room temperature, when the potassium salt of the acid dichloride was formed in good yield, and chlorine was readily replaced by fluorine in this, by interaction with potassium bifluoride solution.

$$K^+(C_6H_5SO_2NPOCl_2)^- + 2KHF_2 \rightarrow K^+(C_6H_5SO_2NPOF_2)^- + 2KCl + 2HF$$

This reaction did not take place with a neutral solution of potassium fluoride. Thus the replacement of chlorine by fluorine in the acid dichlorides of arylsulfonamidophosphoric acids occurs by the action of the $HF_2^-$ ion, and not of the $F^-$ ion, i.e. according to the equation:

$$ArSO_2N{=}PCl_3 + H_2O + 4KF \rightarrow K^+(ArSO_2NPOCl_2)^- + KCl + 2KHF_2 \text{ etc.}$$
$$ArSO_2NHPOCl_2 + 2KF \rightarrow K^+(ArSO_2NPOCl_2)^- + KHF_2 \text{ etc.}$$

The potassium salts of the acid difluorides of phenyl-, p-tolyl-, p-chlorophenyl, p-fluorophenyl- and o-, m- and p-nitrophenylsulfonamidophosphoric acids were obtained by the reaction of trichlorophosphazosulfonaryls with aqueous solutions of potassium fluoride. The products obtained were colorless crystalline compounds, with properties recalling those of the acid dichlorides of the arylsulfonamidophosphoric acids [5]. They are readily soluble in water, with difficulty in methyl and ethyl alcohols, and insoluble in benzene and ether. The potassium salts of the acid difluorides were even more resistant to hydrolysis than those of the acid difluorides. For example, the potassium salts of the acid difluorides could be recrystallized from water heated to 70-80°, though they were hydrolyzed quite rapidly when their aqueous solutions were boiled.

The potassium salts of the acid difluorides of arylsulfonamidophosphoric acids behaved like the salts of the acid dichlorides in reacting with sodium methylate, to give good yields of the methyl esters of the arylsulfonamidophosphoric acids, and this clearly establishes their structures.

$$K^+(ArSO_2NPOF_2)^- + 2CH_3ONa \rightarrow 2NaF + K^+[ArSO_2NPO(OCH_3)_2]^- \xrightarrow[HCl]{} \\ \longrightarrow KCl + ArSO_2NHPO(OCH_3)_2$$

When the potassium salts of the acid difluorides of arylsulfonamidophosphoric acids were heated with potassium fluoride solution, until they had dissolved completely (80-85°), they were partly hydrolyzed to give the dipotassium salts of the acid monofluorides. If the reaction mixture for the fluorination of the acid dichlorides, or of the trichlorophosphazosulfonaryls, was carefully heated on a water bath until the products of the first stage of fluorination (the potassium salts of the acid difluorides) had dissolved, then, on cooling, the dipotassium salts of the acid monofluorides of the arylsulfonamidophosphoric acids separated out in the form of crystalline precipitates. The reaction is as follows:

$$ArSO_2NHPOCl_2 + 7KF + H_2O \rightarrow K_2^+(ArSO_2NPO_2F)^{--} + 2KCl + 3KHF_2.$$

In this way we obtained the dipotassium salts of the acid monofluorides of the p-chlorophenyl-, and o-, m- and p-nitrophenylsulfonamidophosphoric acids. These were colorless crystalline substances, very readily soluble in water and insoluble in organic solvents. The corresponding silver salts were less soluble in water.

The remarkable resistance to hydrolysis, in neutral and alkaline aqueous solution, of the salts of the acid dichlorides [5] and acid difluorides of arylsulfonamidophosphoric acids, of the type $K^+(ArSO_2NPOX_2)^-$ is probably due to the influence of the electronegative substituent $(ArSO_2N)^-$ on the phosphorus atom. Similar cases are described in the literature. For example, it is difficult to hydrolyze the acid dichloride of triphenylmethylphosphinic acid $(C_6H_5)_3CPOCl_2$ [6], or the acid monochloride of trichloromethylphosphinic acid [7], and fairly difficult to hydrolyze the acid dichlorides of arylsulfonamidophosphoric acids $ArSO_2NHPOCl_2$ [2] and the acylamidophosphoric acids $AcNHPOCl_2$ [8]. It is well known that acid dichlorides of phosphoric acids, in which there is no electronegative group attached to the phosphorus atom, hydrolyze very easily. The lower resistance to hydrolysis of the free acid dichlorides of arylsulfonamidophosphoric acids, compared with their salts, is probably due to the greater electronegativity of the $(ArSO_2N)^-$ substituent than of $(ArSO_2NH)$. For the same reason, $CCl_3POCl_2$ hydrolyzes considerably more easily than $CCl_3PO(OH)Cl$ [7].

## EXPERIMENTAL

*Potassium salts of arylsulfonamidophosphoric acids from trichlorophosphazosulfonaryls.* The finely divided trichlorophosphazosulfonaryl (0.01 mole) was added, with stirring, to a saturated aqueous solution of 10.0 g of crystalline potassium fluoride ($KF \cdot 2H_2O$). The temperature rose to 30-40°, and, after a few minutes, the residual trichlorophosphazosulfonaryl was converted into a colorless crystalline deposit of the corresponding potassium salt. Dissolution did not take place, but the form of the new deposit was so characteristic that there was not difficulty in detecting the end of the reaction. After cooling, the product was filtered off under suction, pressed between sheets of filter paper, dried in air and recrystallized. Yields were determined for the pure products (see Table 1).

*Potassium salts of the acid difluorides of phenyl and p-tolylsulfonamidophosphoric acids from acid dichlorides of the corresponding arylsulfonamidophosphoric acids.* A suspension of 0.01 mole of the acid dichloride of the arylsulfonamidophosphoric acid in a saturated solution of 10.0 g of potassium fluoride was heated on a water bath to 30-40°. Dissolution did not occur under these conditions, but the form of the deposit changed markedly and, after a few minutes, crystals of the original substance disappeared as they were converted into a deposit of

TABLE 1

Potassium Salts of Acid Difluorides of Arylsulfonamidophosphoric Acids of the Type $K^+(ArSO_2NPOF_2)^-$

| Aryl | Crystalline form | Solvent for crystallization | Melting point | Yield (%) | Formula | Found, % |  |  | Calculated % |  |  |
|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  | N | K | F | N | K | F |
| $C_6H_5$ | Colorless, lustrous, fine platelets | Ethanol or water | 230—232° | 52.0 | $C_6H_5O_3NSPF_2K$ | 4.95, 5.14 | 14.08, 14.90 | 14.20, 14.53 | 5.01 | 13.62 | 13.96 |
| p $CH_3C_6H_4$ | Platelets | Methanol | 232—235 | 61.0 | $C_7H_7O_3NSPF_2K$ | 5.04, 5.06 | — | 13.37, 13.05 | 4.77 | — | 12.96 |
| p-$ClC_6H_4$ | Platelets | Ethanol or water | 265—268 | 57.0 | $C_6H_4O_3NSPClF_2K$ | 4.20, 4.33 | 12.20, 12.60 | 13.14, 12.74 | 4.46 | 12.44 | 12.12 |
| p-$FC_6H_4$ | Platelets | Ethanol | 225—228 | 35.3 | $C_6H_4O_3NSPF_3K$ | — | — | 19.70 | — | — | 19.19 |
| o-$NO_2C_6H_4$ | Needles | Ethanol | 181—182 | 40.7 | $C_6H_4O_5N_2SPF_2K$ | 8.67, 8.68 | — | — | 8.64 | — | — |
| m-$NO_2C_6H_4$ | Platelets | Ethanol or water | 217—220 | 61.0 | $C_6H_4O_5N_2SPF_2K$ | 8.19, 8.25 | — | — | 8.64 | — | — |
| p-$NO_2C_6H_4$ | Platelets<br>Needles | Aqueous, ethanol, water | 225—228 | 58.0 | $C_6H_4O_5N_2SPF_2K$ | 8.52, 8.60 | — | — | 8.64 | — | — |

the potassium salt. After cooling, the fine colorless crystals of the potassium salt were filtered off under suction and recrystallized from alcohol. The product had the same melting point, and gave no mixed melting point depression with the potassium salt of the acid difluoride of the arylsulfonamidophosphoric acid prepared from the corresponding trichlorophosphazosulfonaryl. The salts were obtained in 40 and 30.7% yields respectively.

Potassium salt of the acid dichloride of phenylsulfonamidophosphoric acid from the acid dichloride of phenylsulfonamidophosphoric acid and potassium fluoride (without heating). The acid dichloride of phenylsulfonamidophosphoric acid (0.01 mole) was added, with vigorous stirring, to a saturated solution of 10.0 g of potassium fluoride, and the reaction mixture was stirred carefully for a further 20 minutes. Dissolution did not occur, but the external form of the deposit changed markedly (see above). The crystalline deposit was filtered off under suction, pressed but not dried, and recrystallized from alcohol. Yield 48.0%. The product was in the form of colorless needles, of m.p. 197-198°, and gave no mixed melting point depression with the potassium salt of the acid dichloride of phenylsulfonamidophosphoric acid, obtained by the action of potash on the acid dichloride of phenylsulfonamidophosphoric acid [5].

Potassium salt of the acid difluoride of phenylsulfonamidophosphoric acid from the potassium salt of the acid dichloride of phenylsulfonamidophosphoric acid and potassium bifluoride. A mixture of 0.005 mole of the potassium salt of the acid dichloride of phenylsulfonamidophosphoric acid with a saturated aqueous solution of 3.0 g of potassium bifluoride was carefully heated on a water bath at 40-50°, until dissolution was complete. After cooling, the product was filtered off under suction and recrystallized from alcohol. Yield 86.0%, m.p. 230-232°. The substance gave no mixed melting point depression with the potassium salt of the acid difluoride of phenylsulfonamidophosphoric acid obtained from trichlorophosphazosulfonphenyl.

TABLE 2

Dimethyl Esters of Arylsulfonamidophosphoric Acids of the Type $ArSO_2HNPO(OCH_3)_2$

| Aryl | Yield,% | Melting point | Literature reference |
|---|---|---|---|
| $C_6H_5$ | 46.0 | 106-108° | [9] |
| $p-ClC_6H_4$ | 68.0 | 128-129 | [5] |
| $m-NO_2C_6H_4$ | 63.0 | 149-150 | [10] |
| $p-NO_2C_6H_4$ | 68.0 | 177-179 | [10] |

Dimethyl esters of arylsulfonamidophosphoric acids. A suspension of 0.005 mole of the potassium salt of the acid difluoride of the arylsulfonamidophosphoric acid in 5.0 ml of methanol was treated with a solution

TABLE 3

Dipotassium Salts of Acid Monofluorides of Arylsulfonamidophosphoric Acids of the Type $K_2^+(ArSO_2NPO_2F)^{--}$

| Aryl | Melting point | Yield (in %) | Formula | Found, % | | | Calculated,% | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | N | K | F | N | K | F |
| $p-ClC_6H_4$ | 312—316° | 46.0 | $C_6H_4O_4NSPClFK_2$ | — | 21.45 | 6.35 | — | 22.31 | 5.43 |
| $o-NO_2C_6H_4$ | 235—237 | 77.0 | $C_6H_4O_6N_2SPFK_2$ | 7.85,<br>7.75 | — | — | 7.77 | — | — |
| $m-NO_2C_6H_4$ | 302—306 | 73.0 | $C_6H_4O_6N_2SPFK_2$ | 8.03,<br>8.04 | — | 5.69,<br>5.94 | 7.77 | — | 5.27 |
| $p-NO_2C_6H_4$ | 299—302 | 37.0 | $C_6H_4O_6N_2SPFK_2$ | 7.74,<br>7.74 | — | 6.62 | 7.77 | — | 5.27 |

of 0.01 mole of sodium methylate in 15.0 ml of methanol. After 1 hour, the methanol was distilled off under reduced pressure and the residue was dissolved in water. The aqueous solution was filtered and acidified with hydrochloric acid. The diester precipitated was filtered off under suction and recrystallized. The dimethyl esters, prepared in this way, gave no mixed melting point depression with samples prepared from the corresponding arylsulfonamidophosphoric acids (Table 2).

Dipotassium salts of acid monofluorides of arylsulfonamidophosphoric acids. The trichlorophosphazosulfonaryls or acid dichlorides of the arylsulfonamidophosphoric acid, (0.01 mole) were added slowly, with stirring, to a saturated solution of 10.0 g of crystalline potassium fluoride. The reaction mixture was heated on a water bath, until the deposit had dissolved completely and then for a few minutes further, at 80-85°. The product, which came down on cooling, was filtered off under suction and recrystallized from aqueous alcohol. Yields were determined for the crystallized materials (Table 3). All the dipotassium salts obtained crystallized from aqueous alcohol in the form of platelets.

## SUMMARY

By the action of trichlorophosphazosulfonaryls, or of acid dichlorides of arylsulfonamidophosphoric acids, on a saturated aqueous solution of potassium fluoride, according to the conditions of the reaction, there were obtained, successively, the potassium salts of the acid dichlorides, the potassium salts of the acid difluorides and the dipotassium salts of the acid monofluorides, of arylsulfonamidophosphoric acids. The structures of the potassium salts of the acid difluorides were confirmed by conversion of the latter to the corresponding methyl esters, by reaction with sodium methylate. It was shown that the potassium salts of the acid difluorides were even more resistant to hydrolysis than the potassium salts of the acid dichlorides, and the reason for this was discussed.

## LITERATURE CITED

[1] A. V. Kirsanov, J. Gen. Chem. 22, 269 (1952).*

[2] A. V. Kirsanov and E. A. Abrazhanova, J. Gen. Chem. Supp. II, 1048 (1953).

[3] A. V. Kirsanov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 426 (1950); 710 (1952).*

[4] German Patent 664,438; Frdl. 25,1313 (1913).

[5] E. S. Levchenko and A. V. Kirsanov, J. Gen. Chem. 27,3078 (1957).*

[6] A. E. Arbuzov and B. A. Arbuzov, J. Russ. Chem. Soc. 61, 22 (1929).

[7] A. Ia. Iakubovich and V. A. Ginsburg, J. Gen. Chem. 24, 2251 (1954).*

[8] A. V. Kirsanov and R. G. Makitra, J. Gen. Chem. 26, 905 (1956).*

[9] A. V. Kirsanov and V. I. Shevchenko, J. Gen. Chem. 24, 882 (1954).*

[10] A. V. Kirsanov and N. G. Feshchenko, J. Gen. Chem. 27, 2817 (1957).*

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# DIPHENYLAMIDES OF TRICHLOROPHOSPHAZOCARBONIC ACIDS AND THEIR DERIVATIVES

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There is at present only one method known for preparing derivatives of the N-phosphoric acids of urea (carbamidophosphoric acids), namely the addition of primary or secondary amines to the chloroanhydrides or esters of isocyanatophosphoric acid [1]. Moreover, the product of the reaction of phosphorus pentachloride with urea is bistrichlorophosphazocarbonyl [2], which is a derivative of N,N'-carbamidobisphosphoric acid. In order to develop a general method for obtaining N,N-disubstituted carbamido-N'-phosphoric acids and their derivatives, and at the same time to extend the range of use of the reaction of phosphorus pentachloride with the amides of acids, we have investigated the reaction between phosphorus pentachloride and N,N-diphenylurea.

In carbon tetrachloride solution, at 70-80°, phosphorus pentachloride reacted almost quantitatively with N,N-diphenylurea to give the diphenylamide of trichlorophosphazocarbones acid, in accordance with the equation

$$(C_6H_5)_2NCONH_2 + PCl_5 \rightarrow 2HCl + \underset{(I)}{(C_6H_5)_2NCON{=}PCl_3}$$

The diphenylamide of trichlorophosphazocarbonic acid (I) was analogous, on the one hand, to the recently obtained trichlorophosphazoacyls [3], and, on the other hand, to the dialkylamides of trichlorophosphazosulfuric acid [4].

(I) was a low-melting crystalline material, which could only be distilled without decomposition in a high vacuum, readily hydrolyzed by water, and reacting vigorously with alcohols, phenols and amines. Under the action of anhydrous formic acid, depending on the conditions, (I) gave all the theoretically possible phosphorus-containing hydrolysis products, namely – the dichloroanhydride of N,N-diphenylcarbamido-N'-phosphoric acid $(C_6H_5)_2NCONHPOCl_2$ (II), the monochloroanhydride of N,N-diphenylcarbamido-N'-phosphoric acid

$$(C_6H_5)_2NCONHPO(OH)Cl \quad (III)$$

and free N,N-diphenylcarbamido-N'-phosphoric acid

$$(C_6H_5)_2NCONHPO(OH)_2 \quad (IV).$$

Further hydrolysis gave diphenylamine, carbon dioxide and phosphaminic acid.

(II), obtained from (I), was found to be identical with the product of addition of diphenylamine to the chloroanhydride of isocyanatophosphoric acid [1], which, together with the means of preparation and the analytical data, rigidly proved the structures (II) and (I).

(I) was hydrolyzed by the action of water vapor in $CCl_4$ solution to give (II), and in benzene or dioxane solution to give (III). (II), (III) and (IV) were crystalline compounds with properties recalling those of the hydrolysis products of trichlorophosphazosulfon compounds [5] and of trichlorophosphazoacyls [6], although from the latter, in spite of its resemblance to (I), it has not yet been possible to obtain hydrolysis products of type (III), i.e. monochloroanhydrides of acylamidophosphoric acids. (II) hydrolyzed with considerably more difficulty than (I), and (III) with more difficulty then (II). The reason for this has been discussed in a previous paper [7].

On reaction with sodium arylates, (I) gave satisfactory yields of the diphenylamides of the corresponding triaroxyphosphazocarbonic acids, of the type $(C_6H_5)_2NCON{=}P(OAr)_3$ (V), and these were low-melting crystalline substances or viscous liquids of a neutral character. The chemical properties of (V) were intermediate between, on the one hand, the triaroxyphosphazosulfon-aryls [8], or -alkyls [9], and, on the other hand, the triaroxyphosphazotrichloroacetyls [10] and the triaroxyphosphazoacyls of the aromatic series [7]. The latter can only be obtained under conditions of complete exclusion of moisture; on shaking with water at room temperature, or on storage in air, they are rapidly hydrolyzed to the diesters of acylamidophosphoric acids [7]. The triaroxyphosphazotrichloroacetyls [10] hydrolyze with rather more difficulty. The diphenylamides of the triaroxyphosphazocarbonic acids (V) hydrolyzed much more easily than the triaroxyphosphazosulfoncompounds [8], but with much more difficulty than the triaroxyphosphazoacyls of the aromatic series and of the trichloracetic acid class [7, 10]. For this reason, (V) could be synthesized under normal conditions, and their solutions in nonpolar solvents could be washed with water and weak alkali (like triaroxyphosphazosulfon compounds), but they hydrolyzed easily on boiling with 96% alcohol in the absence of alkali, or on prolonged agitation of their solutions in nonpolar solvents with water at room temperature (like the triaroxyphosphazoacyls). Thus the rate of hydrolysis of triaroxyphosphazoacyls of the type $AcN=P(OAr)_3$ markedly increases along the Ac series:

$$RSO_2 < (C_6H_5)_2NCO < CCl_3CO < ArCO$$

The reason for the relative difficulty of hydrolysis of the triaroxyphosphazosulfon compounds, as compared with the triaroxyphosphazoacyls, has been previously discussed [7]. The probable explanation of the relative resistance to hydrolysis of the diphenylamides of triaroxyphosphazocarbonic acids (as compared with other triaroxyphosphazocarbacyls) is that, in the series Ac, ArCO, $CCl_3CO$, $(C_6H_5)_2NCO$, for the given type of compound, the $(C_6H_5)_2N$ group is the most electronegative, and therefore "interferes" most with the conjugation of the bonds $O=C$ and $N=P$, i.e. it most reduces the electrophilic character of the phosphorus atom, and therefore reduces the rate of hydrolysis.

As with all other types of triaroxyphosphazocompounds, hydrolysis of the diphenylamides of trinitrotriphenoxyphosphazocarbonic acid: (IX and X) took place much more easily (by the action of 96% ethanol at room temperature) than that of the diphenylamides of a triaroxyphosphazocarbonic acid without electronegative substituents in the aroxy groups.

Hydrolysis of the diphenylamide of a triaroxyphosphazocarbonic acid (V) affected not only the $N=P$ linkage, but also the C-N bond so that, as well as the diester of the N,N-diphenylcarbamido-N'-phosphoric acid, 10-20% of diphenyl was always obtained. Hydrolysis of the C-N bond was complete when (V) was boiled, in aqueous alcohol solution, with 2 equiv. of caustic alkali.

The diaryl esters of N,N-diphenylcarbamido-N'-phosphoric acid were colorless crystalline substances, melting at a lower temperature than the diphenylamides of the corresponding triaroxyphosphazocarbonic acids, titrating with caustic alkali as monobasic acids in the presence of phenolphthalein, and decomposing on boiling with alkali to give diphenyl and the esters of phosphaminic acids. The remaining properties of the compounds obtained are described in the experimental part.

## EXPERIMENTAL

Diphenylamide of trichlorophosphazocarbonic acid (I). A mixture of 0.01 mole of carefully dried and powdered N,N-diphenylurea, 0.01 mole of phosphorus pentachloride and 50.0 ml of $CCl_4$ was heated with stirring under a reflux condenser, on a water bath at 70-80°. The evolution of hydrogen chloride began immediately and the reactants gradually went into solution. All had dissolved after 30 minutes, and the evolution of hydrogen chloride slackened. The hot solution was filtered after 45 minutes, and the bulk of the solvent was distilled off, under reduced pressure, at 35-40°. The substance (I) precipitated, after cooling, in the form of fine colorless needles, which were filtered off under suction, washed with $CCl_4$ and dried in vacuo. The mother liquor was evaporated to a small volume and the (I) precipitated was filtered off. The total yield was about 100%, of m.p. 112-114°. The hydrogen chloride liberated in the reaction was absorbed in water and titrated. Yield about 100%. (I) was easily soluble in acetone and dioxane, with difficulty in benzene and $CCl_4$, and with great difficulty in ether and petroleum ether.

Found %: Cl 30.09. Equiv. after hydrolysis 5.08, 5.06. $C_{13}H_{10}ON_2PCl_3$. Calculated %: Cl 30.66 Equiv. after hydrolysis 5.00.

Dichloroanhydride of N,N-diphenylcarbamido-N'-phosphoric acid (II). a) Obtained from (I) by the action of HCOOH. A solution of 0.01 mole of (I) in 30.0 ml of benzene was treated with a solution of 0.01 mole of anhydrous HCOOH in 20.0 ml of benzene. A vigorous evolution of CO and HCl began immediately, and (II) was precipitated from the solution in the form of fine, colorless, transparent prisms. The reaction was complete after 20-30 minutes; the (II) was filtered off under suction, washed with benzene and dried in vacuo. The total yield was about 95%, m.p. 136-137° (decomp.). (II) was readily soluble in acetone, chloroform, dioxane and dichloroethane, dissolved on boiling in benzene and $CCl_4$, and was insoluble in ether and petroleum ether.

Found %: Cl 21.19, 21.32. Equiv. after hydrolysis 3.98, 3.98. $C_{13}H_{11}O_2N_2PCl_2$. Calculated %: Cl 21.58. Equiv. after hydrolysis 4.00

In a previous paper [11], the analytical data and melting points in the table were transposed for the dichloroanhydrides of N,N-diphenylcarbamido-N'-phosphoric acid and N,N-phenylethylcarbamido-N'-phosphoric acid. It should be noted that the m.p. of the former is 136-137° (decomp.) and of the latter 113-114° (decomp.).

b) Preparation from the chloroanhydride of isocyanatophosphoric acid and diphenylamine (Cf. [11]). A solution of 0.02 mole of diphenylamine in 10.0 ml of benzene was added slowly, with cooling (from + 5 to +10°) and stirring, to a solution of 0.02 mole of the chloroanhydride of isocyanatophosphoric acid in 10.0 ml of benzene. After 30 minutes, the crystalline precipitate formed was filtered off under suction, washed with benzene, dried in vacuo and recrystallized from $CCl_4$. The total yield (including recovery from the mother liquor) of about 91%, m.p. 136-137°, gave no mixed melting point depression with (II) obtained by method a).

c) Preparation from (I) by the action of water vapor. Three beakers, half filled with solutions of (I) in benzene, dioxane and $CCl_4$, and a fourth beaker of water, were placed in a desiccator. The surfaces of the solutions gradually became covered with crystals, and these soon filled the whole volume of liquid. They were filtered off under suction after 3 hours, and washed with the corresponding solvent. The yields were variable and not good. The product, precipitated from $CCl_4$, was identified as (II) by its m.p. of 132-136° and mixed melting point. The products, precipitated from benzene and dioxane, were identified as (III) by their m.p. of 171-174°, by mixed melting point and by titration.

Monochloroanhydride of N,N-diphenylcarbamido-N'-phosphoric acid (III). A solution of 0.01 mole of anhydrous HCOOH in 50.0 ml of benzene was added to a boiling solution of 0.01 mole of (II) in 50.0 ml of benzene, and the mixture was boiled under a reflux condenser for 1 hour. By then more than 100% of hydrogen chloride (absorbed in water and titrated) had been evolved. After a day, the precipitate of (III) (an aggregate of fine prisms) was filtered off under suction, washed with warm benzene and dried in vacuo. Yield 61.9%, m.p. 172-176° (decomp.). (III) was readily soluble in dioxane and chloroform, but insoluble in benzene, $CCl_4$, ether and petroleum ether; it was readily soluble in water and alcohol (with decomposition).

Found %: Cl 11.19; Equiv. after hydrolysis 3.08, 3.07. $C_{13}H_{12}O_3N_2PCl$. Calculated %: Cl 11.43. Equiv. after hydrolysis 3.00.

N,N-diphenylcarbamido-N'-phosphoric acid (IV). A mixture of 0.03 mole of HCOOH and 20.0 ml of benzene was added slowly, with vigorous stirring, to a solution of 0.01 mole of (I) in 50.0 ml of benzene. The reaction went vigorously at the start, but ceased after 15 minutes. The mixture was then boiled for 4 hours under a reflux condenser. By this time about 90% of the hydrogen chloride had been evolved. The precipitate formed on cooling was filtered off under suction, washed with warm benzene and dried in vacuo. Yield 63.7%. The product was a fine crystalline powder which decomposed with swelling at 110°, deliquesced in air, was readily soluble in water, but with difficulty in alcohol, was insoluble in nonpolar solvents, and did not contain chlorine.

Found %: 2.03. $C_{13}H_{13}O_4N_2P$. Calculated %: Equiv. 2.00.

Diphenylamide of triphenoxyphosphazocarbonic acid (VI). A solution of 0.02 mole of (I) in 50.0 ml of benzene was added with vigorous stirring to a suspension of 0.06 mole of dry sodium phenate in 50.0 ml of benzene. Considerable heat was evolved and the form of the suspended matter altered. The reaction mixture was boiled with stirring under a reflux condenser for 30 minutes, cooled to 0° and shaken vigorously with 50.0 ml of 0.2 N caustic soda (precooled to 0°); the benzene solution was quickly separated, washed three times with ice water and filtered through two funnels, one above the other, each containing a filter paper and 3 g of anhydrous sodium sulfate. The more quickly these operations were carried out, the greater was the yield of VI. The benzene solution was evaporated under reduced pressure, leaving a residue, VI, in the form of a colorless transparent liquid. Yield about 90%. This nearly all crystallized after a day. The crystals were pressed, washed with petroleum ether and dried in vacuo. The product was a colorless material, of a neutral character, crystallizing in the form of fine plates, of m.p. 83-84°, readily soluble in benzene, alcohol, dichloroethane, acetone, ether and $CCl_4$; it dissolved in petroleum ether on heating with aqueous alcohol to give the diphenyl ester of N,N-diphenylcarbamido-N'-phosphoric acid.

Found %: N 5.16, 5.55. $C_{31}H_{25}O_4N_2P$. Calculated %: N 5.39.

Diphenylamide of tri-p-chlorotriphenoxyphosphazocarbonic acid (VII) A solution of 0.02 mole of I in 20.0 ml of benzene was added with vigorous stirring to a solution of 0.06 mole of sodium p-chlorophenate in 120 ml of ether. When the vigorous reaction had finished, the mixture was boiled under a reflux condenser, for 15 minutes. Subsequent treatment was the same as for VI. The yield was about 80%. The product crystallized in the form of fine needles of m.p. 128-130° and was readily soluble in benzene, ether, dioxane, dichloroethane, chloroform and acetone, dissolved on boiling in alcohol and $CCl_4$, and with difficulty in boiling petroleum ether.

Found %: N 4.41. $C_{31}H_{22}O_4N_2PCl_3$. Calculated %: 4.49.

The diphenylamide of tri-o-chlorotriphenoxyphosphazocarbonic acid (VIII) was obtained in the same way as VII. The yield was about 80%. (VIII) crystallized with great difficulty in the form of fan-shaped aggregates of needles, of m.p. 40-43°, and was readily soluble in ether and benzene, and with difficulty in $CCl_4$, acetone, chloroform and dichloroethane; it dissolved with difficulty in boiling petroleum ether.

Found %: N 4.51, 4.59. $C_{31}H_{22}O_4N_2PCl_3$. Calculated %: N 4.49.

Diphenylamide of tri-o-nitrotriphenoxyphosphazocarbonic acid (IX) The reaction was carried out in the same way as for (VI). Precipitated sodium chloride and a small quantity of nitrophenate were filtered off under suction and the benzene solution was boiled with active carbon the carbon was filtered off; and the benzene solution was evaporated under reduced pressure at 40°. The residue was in the form of a yellow oil (yield 83.9%). This dissolved readily in benzene, chloroform, dichloroethane, dioxane, acetone and $CCl_4$, but was insoluble in ether and petroleum ether. It hydrolyzed to (XV) on shaking with 96% ethanol.

Found %: N 10.81, 10.84. $C_{31}H_{22}O_{10}N_5P$. Calculated %: N 10.69.

Diphenylamide of tri-o-nitrotriphenoxyphosphazocarbonic acid (X) The reaction was carried out as for (VI), but it was necessary to boil the mixture with stirring under a reflux condenser for 8 hours. Subsequent treatment was the same as for (IX). Yield 91.4%. The product was a thick, very viscous, dark yellow oil; it was readily soluble in benzene, chloroform, dichloroethane, dioxane and acetone, and dissolved on heating in $CCl_4$, but was insoluble in ether and petroleum ether. It hydrolyzed to (XV) on shaking with 96% ethanol.

Found %: N 10.49, 10.70. $C_{31}H_{22}O_{10}N_5P$. Calculated %: N 10.69.

(IX) and (X) hydrolyzed considerably more easily than (VI-VIII); for this reason, treatment with aqueous solutions is not recommended in the isolation of (IX) and (X).

Diphenylamide of tri-α-naphthoxyphosphazocarbonic acid (XI). This was obtained in the same way as (VII). Yield about 70%. The product was a colorless, glass-like material, of m.p. 47-50°, readily soluble in ether, benzene, acetone, chloroform and dichloroethane, but insoluble in petroleum ether.

Found %: N 4.21. $C_{43}H_{31}O_4N_2P$. Calculated %: N 4.18.

Diphenyl ester of N,N-diphenylcarbamido-N'-phosphoric acid (XII) A mixture of 0.01 mole of (VI) and 50.0 ml of 96% ethanol was boiled, under a reflux condenser for 2 hours. (XII) deposited on cooling, in the form of coarse transparent prisms with truncated angles. The product was filtered off under suction, washed with alcohol and dried in vacuo. Yield 74.3%, m.p. 147-149°.

Found %: N 6.38. Equiv. 1.02. $C_{25}H_{21}O_4N_2P$. Calculated %: N 6.30. Equiv. 1.00.

Diphenylamine (13.6%) was recovered from the mother liquor and identified by mixed melting point.

Di-p-chlorodiphenyl ester of N,N-diphenylcarbamido-N'-phosphoric acid (XIII). This was obtained in the same way as (XII). The yield was 55.2%, of m.p. 151-152°, and the material crystallized from ethanol in the form of fine needles.

Found %: N 5.60. Equiv. 0.990. $C_{25}H_{19}O_4N_2PCl_2$. Calculated %: N 5.46. Equiv. 1.000.

Di-o-chlorodiphenyl ester of N,N-diphenylcarbamido-N'-phosphoric acid (XIV). This was obtained in the same way as (XII). The yield was 41.4%, of m.p. 63-65°, and the product crystallized from ethanol in the form of fine prisms.

Found %: N 5.56, 5.71. Equiv. 0.994, 0.998. $C_{25}H_{19}O_4N_2PCl_2$. Calculated %: N 5.46, Equiv. 1.000.

Substances (XII-XIV) were readily soluble in acetone and chloroform, and in boiling benzene, alcohol and $CCl_4$, but were insoluble in ether and petroleum ether; they could be titrated with caustic alkali as monobasic acids, in the presence of phenophthalein.

Di-p-nitrodiphenyl ester of N,N-diphenylcarbamido-N'-phosphoric acid (XV). 0.01 mole of (IX) was shaken vigorously with 50.0 ml of 96% ethanol. The oily (IX) dissolved rapidly, and, at the same time (XV) precipitated in the form of fine crystals. The product was filtered off under suction, washed with alcohol and dried in vacuo. Yield 72.1%, m.p. 148-150°.

Found %: N 10.51. Equiv. 1.004. $C_{25}H_{19}O_8N_4P$. Calculated %: N 10.49. Equiv. 1.000.

Di-o-nitrodiphenyl ester of N,N-diphenylcarbamido-N'-phosphoric acid (XVI). This was obtained in the same way as (XV). The yield was 31.8%, of m.p. 182-183°, and the product crystallized in the form of fine prisms.

Found %: N 10.55, 10.72. Equiv. 1.005, 0.980. $C_{25}H_{19}O_8N_4P$. Calculated %: N 10.49. Equiv. 1.000.

(XV) and (XVI) were readily soluble in acetone and dioxane, and in boiling alcohol, benzene, dichloroethane and chloroform, but were insoluble in ether, petroleum ether and $CCl_4$.

Hydrolysis of (V) with 2 equiv. of caustic alkali. A mixture of 0.005 mole of (V) with 20.0 ml of ethanol and 10.0 ml of N aqueous sodium hydroxide was boiled under a reflux condenser for 2 hours. The alcohol was distilled off under reduced pressure, whereupon the diphenyl precipitated from the aqueous solution in the form of crystals. The yield was quantitative. The product was identified by the mixed melting point method.

## SUMMARY

The reaction of phosphorus pentachloride with N,N-diphenylurea has been investigated. The diphenylamide of trichlorophosphazocarbonic acid was obtained together with all its possible hydrolysis products (without degradation).

Diphenylamides of triaroxyphosphazocarbonic acids and diaryl esters of N,N-diphenylcarbamido-N'-phosphoric acids were obtained and their properties described.

## LITERATURE CITED

[1] A. V. Kirsanov, J. Gen. Chem. 24, 1033 (1954); A. V. Kirsanov and E. S. Levchenko, J. Gen. Chem. 26, 2285 (1956);* 27, 2585 (1957);* A. V. Kirsanov and I. N. Zhmurova, J. Gen. Chem. 27, 1002 (1957).*

[2] A. V. Kirsanov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 646 (1954).*

[3] A. V. Kirsanov and R. G. Makitra, J. Gen. Chem. 27, 3241 (1957).*

[4] A. V. Kirsanov and Z. D. Nekrasova, J. Gen. Chem. 27, 3241 (1957).*

[5] A. V. Kirsanov and E. A. Abrazhanova, J. Gen. Chem. Supplement II, 1048 (1953).

[6] A. V. Kirsanov and R. G. Makitra, J. Gen. Chem. 26, 905 (1956).*

[7] A. V. Kirsanov, R. I. Derkach and R. G. Makitra, J. Gen. Chem. 28, 1227 (1958).*

[8] A. V. Kirsanov and V. I. Shevchenko, J. Gen. Chem. 24, 474 (1954);* A. V. Kirsanov and R. G. Makitra, J. Gen. Chem. 27, 245 (1957);* A. V. Kirsanov and N. G. Feshchenko, J. Gen. Chem. 28, 2817 (1957).*

---

*Original Russian pagination. See C.B. Translation.

[9] A. V. Kirsanov and N. L. Egorova, J. Gen. Chem. 28, 1052 (1958).*

[10] A. V. Kirsanov and G. I. Derkach. J. Gen. Chem. 26, 2631 (1956).*

[11] A. V. Kirsanov and E. S. Levchenko, J. Gen. Chem. 26, 2286 (1956).*

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* Original Russian pagination. See C.B. Translation.

# 2,4-DI-(ETHYLENEIMINO)-1,3,5-TRIAZINES

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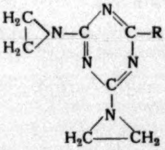
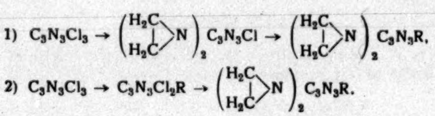
Among 1,3,5-triazine derivatives, great interest attaches to 2,4,6-triethyleneimino-1,3,5-triazine as a possible drug for the treatment of some forms of cancer. The interesting physiological properties of this substance have attracted the attention of investigators, with the result that a large number of similar compounds have been prepared, and much new information has been obtained on the chemistry of the ethyleneiminotriazines.

In the search for improved therapeutic agents for the treatment of cancer, we undertook the synthesis of 2,4-di-(ethyleneimino)-1,3,5-triazines having as a third substituent (R) in the triazine ring either a nitrogen-containing heterocyclic radical or the groupings of the esters of aliphatic or arylaliphatic amino-acids.



To prepare the substituted 1,3,5-triazines, the starting material was usually cyanuric chloride, in which the chlorine atoms were all or partly replaced by other groups of radicals. The substituents could be introduced in various ways, depending on the nature of the reagent and the reaction conditions [1]. Two means of synthesis could be used: 1) starting from the known substance 2,4-di-(ethyleneimino)-6-chloro-1,3,5-triazine, and replacing the chlorine in it by the corresponding amino compound, or 2) starting from cyanuric chloride, replacing only one chlorine atom by the amino compound, and then allowing the substituted 2,4-triazine to react with ethyleneimine



We used both methods.

Compounds containing heterocyclic radicals (morpholyl, piperazyl and methylpiperazyl derivatives) were obtained by the first method, but 2,4-di-(ethyleneimino)-6-piperidyl-1,3,5-triazine by the second. In all cases, the reaction was carried out in an anhydrous solvent (benzene or ether) and triethylamine was used to fix the hydrogen chloride evolved. As would be expected, both the imino groups of piperazine reacted; the bis-[2,4-di-(ethyleneimino)-1,3,5-triazine-6]- piperazine formed was insoluble in water and most organic solvents, and was unsuitable for biological investigations. Attempts to obtain a singly substituted piperazine, by specially selected conditions of the reaction, were unsuccessful. The introduction of amino-acid groups into the 1,3,5-

triazine ring was more complicated. The replacement of chlorine by an amino-acid group in 2,4-di-(ethylene imino)-6-chloro-1,3,5-triazine, or even in cyanuric chloride, did not take place, in spite of the use of different conditions of reaction. If esters were used instead of free amino-acids, successful results were only obtained if the ester was first allowed to react with cyanuric chloride, and ethyleneimino groups were then introduced into the product.

The details of the stages of the preparations varied from case to case; but it is possible to make some generalizations. The solvents used were anhydrous benzene, ether or methylene chloride. In the reaction of cyanuric chloride with amino-acid esters, the temperature conditions varied from 5-10° (exp. 5 and 6), room temperature (exp. 7, 8, 11, 13) to 30-40° (exp. 9). The reaction of 6-substituted 2,4-dichloro-1,3,5-triazines with ethyleneimine was always carried out in the cold (5-10°). Triethylamine was used in some cases (exp.5 and 6) for fixing the hydrogen chloride in both the first and second stages of the preparation. But the use of this amine was not essential, and it was more convenient to use twice the theoretical quantity of the amino-acid ester in the first stage, and of ethyleneimine in the second stage; under these conditions, the hydrochlorides of these reagents precipitated almost quantitatively from the anhydrous solvents, and the corresponding triazine derivative remained in solution.

In the first stage it was helpful, and sometimes necessary, to seed the mixture at the beginning of the reaction with a few crystals of the hydrochloride of the corresponding amino-acid ester.

For the most part, the 6-substituted 2,4-dichloro-1,3,5-triazines were well crystallized; some of them were isolated, purified and analyzed (exp. 5,7,11), others were used for subsequent reactions without any special purification; it was also possible to dispense with their isolation and, after carrying out the reaction with cyanuric chloride, to add ethyleneimine to the solution of the substituted dichlorotriazine (exp. 8). The interaction of 6-substituted 2,4-dichloro-1,3,5-triazines with ethyleneimine took place at different speeds, depending on the structure of amino-acid; the reaction was slower the greater the molecular weight of the amino-acid. The completion of the reaction could be judged by a negative reaction of the solution for chlorine (Beilstein). The amino-acid esters required were obtained by the action of gaseous ammonia on suspensions of their hydrochlorides in ether. The yields were 80-90%. Other methods described in the literature for isolating amino-acid esters from their hydrochlorides gave too low a yield.

Since diethyleneiminotriazine derivatives containing free amino-acid groups were of special interest for biological investigations, we attempted to achieve their synthesis in another way; namely: to use compounds containing an amino-acid benzyl ester group, and to split off the benzyl group by hydrogenation. The hydrogenation of these compounds was carried out under different conditions: using xylene, ethylacetate, alcohol and other solvents, temperatures from room temperature to 90°, hydrogen pressures from atmospheric up to 60 atm., palladium, palladium on charcoal and supported nickel as catalysts. But, under the milder conditions, the starting material was recovered unchanged, and under the more drastic conditions there was isomerization of the ethyleneimine ring; this was in agreement with some data in the literature [2].

The biological activities of the compounds prepared by us will be described elsewhere, but it may be stated that (according to the results of V. A. Chernov) their general biological properties were very similar to those of triethyleneiminotriazine, but none of them showed any special features or advantages, as compared with the ethyleneimino compounds used in clinical medicine.

## EXPERIMENTAL

1. 2,4-Di-(ethyleneimino)-6-morpholyl-1,3,5-triazine. A solution of 0.65 g of morpholine in 10 ml of anhydrous benzene was added, drop by drop, at room temperature, with stirring, to a solution of 1.5 g of 2,4-di-(ethyleneimino-)-6-chloro-1,3,5-triazine and 0.76 g of triethylamine in 50 ml of anhydrous benzene. Stirring was then continued for a further 1.5 hours, and the precipitated triethylamine hydrochloride (1.03 g) was filtered off; the solvent was distilled off from the filtrate under reduced pressure. The yield was 1.4 g of a substance of m.p. 121-123°. The m.p. was 135-136° after recrystallization from ethyl acetate. The product was soluble in water, alcohol, ether and benzene.

Found %: C 53.00; H 6.36; N 34.10. $C_{11}H_{16}ON_6$. Calculated %: C 53.21; H 6.47; N 33.89.

2. N-2,4-[Di-(ethyleneimino)-1,3,5-triazyl]-$N'$-methylpiperazine. The reaction was carried out in solution in anhydrous ether at room temperature. The reactants were 1.58 g of 2,4-di-(ethyleneimino)-6-

chloro-1,3,5-triazine in 60 ml of ether and 1.6 g of methylpiperazine in 20 ml of ether. After adding the methylpiperazine, the reaction mixture was stirred for 4 hours and then allowed to stand until the next day. After filtration, the ether was distilled off from the solution under reduced pressure, to give 1.8 g (85.4%) of a substance of m.p. 78-82°. After recrystallization from anhydrous ether, the m.p. was 82.5-83.5°. The product was soluble in water, alcohol, ether and benzene.

Found %: C 54.60; H 7.30; N 37.23. $C_{12}H_{21}N_7$. Calculated %: C 54.74; H 8.04; N 37.23.

3. N,N'-Di-[2,4-di-(ethyleneimino)-1,3,5-triazyl]-piperazine. The reaction was carried out in solution in dry methylene chloride at room temperature. The reactants were 1 g of 2,4-di-(ethyleneimino)-6-chloro-1,3,5-triazine, 0.51 g of triethylamine in 40 ml of methylene chloride and 0.21 g of piperazine in 10 ml of methylene chloride. The next day, the methylene chloride was distilled off from the reaction mixture, and the remaining colorless deposit (1.7 g) was extracted 3 times with methyl alcohol. The insoluble residue (0.9 g) gave no reaction for halogen. Yield 90.5%. The product did not melt on heating to 350°, and was insoluble in water, alcohol, ether or benzene.

Found %: C 53.12; H 5.83; N 41.39. $C_{18}H_{24}N_{12}$. Calculated %: C 52.93; H 5.92; N 41.15.

4. 2,4-Di-(ethyleneimino)-6-piperidyl-1,3,5-triazine. a) 2,4,-Dichloro-6-piperidyl-1,3,5-triazine. A solution of 2.8 g of piperidine and 3.34 g of triethylamine in 20 ml of anhydrous benzene was added to a solution of 6.1 g of cyanuric chloride in 125 ml of anhydrous benzene, the temperature of the reaction mixture being kept below 5-7°. After the addition, the reaction mixture was stirred for 3-4 hours at room temperature, and allowed to stand until the nest day. The triethylamine hydrochloride was filtered off, and the benzene was distilled off from the filtrate under reduced pressure. The remaining slightly yellow, oil was dissolved in 25 ml of ethyl acetate. The solution was filtered, and the filtrate was distilled under reduced pressure until the volume remaining was 2-3 ml. The crystals deposited were filtered off and washed with ethyl acetate. M.p. 90-91°.

Found %: Cl 30.30, 30.70. $C_8H_{10}N_4Cl_2$. Calculated %: Cl 30.42.

b). 2,4-Di-(ethyleneimino)-6-piperidyl-1,3,5-triazine. A solution of 0.37 g of ethyleneimine and 0.87 g of triethylamine in 50 ml of anhydrous benzene was added gradually, with stirring, to a solution of 1 g of 2,4-dichloro-6-piperidyl-1,3,5-triazine in 25 ml of anhydrous benzene, at 5-6°. The reaction mixture was then stirred for 4 hours at room temperature and allowed to stand until the next day. The triethylamine hydrochloride was filtered off, and the benzene was distilled off from the filtrate under reduced pressure at a temperature below 40°. The residue was dissolved in anhydrous ether. The ethereal solution was stirred up with carbon and filtered; the ether was distilled off from the filtrate under reduced pressure at room temperature. A colorless crystalline product was obtained, with a m.p. of 122° (determined by lowering a capillary into the apparatus, heated to 120°). The crystals were purified by two recrystallizations from ethyl acetate. M.p. 130.5-131.5°.

Found %: C 58.42, 58.54; H 7.32, 7.40; N 34.18, 34.22. $C_{12}H_{18}N_6$. Calculated %: C 58.51; H 7.36; N 34.12.

5. Ethyl ester of N-[2,4-di-(ethyleneimino)-1,3,5-triazyl-6-]-aminoacetic acid. a) Ethyl ester of aminoacetic acid. A stream of ammonia was passed through a suspension of 5 g of the hydrochloride of aminoacetic acid ethyl ester* in anhydrous ether cooled by ice water. Ammonium chloride was filtered off, the ether was evaporated, and the residue was distilled under reduced pressure. B.p. 76.5° at 50 mm. Yield 3.36 g (91%).

The same method was used for obtaining the following amino-acid esters – methyl ester of D,L-alanine, b.p. 59° at 48 mm; ethyl ester of D,L-alanine, b.p. 58° at 45 mm; benzyl ester of D,L-alanine, b.p. 119-121° at 7 mm; methyl ester of $\beta$-aminopropionic acid, b.p. 69° at 58 mm; ethyl ester of D,L-$\alpha$-aminoisovaleric acid, b.p. 91.5° at 38 mm; diethyl ester of D,L-aspartic acid, b.p. 136-137° at 15 mm; diethyl ester of D,L-glutamic acid, b.p. 126-128° at 7 mm.

b) Ethyl ester of N-(2,4-dichloro-1,3,5-triazyl-6)-aminoacetic acid. A solution of 2.38 g of the ethyl ester of glycine and 2.34 g of triethylamine in 20 ml of anhydrous benzene was added, drop by drop, with stirring, to a solution of 4.26 g of cyanuric chloride in 100 ml of anhydrous benzene, at 6-8°. The subsequent procedure was as in. 4. After the benzene had been distilled off, the residual oil was dissolved in dry ether, and the solution was treated with carbon and filtered. The ether was distilled off, leaving 3.66 g of colorless crystals, which were washed with petroleum ether and recrystallized from anhydrous ether. M.p. 88-89°.

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*Prepared by Fischer's method [3].

Found %: C 33.45; H 3.14; N 22.66. $C_7H_8N_4O_2Cl_2$. Calculated %: C 33.48; H 3.21; N 22.32.

c) A solution of 0.86 g of ethyleneimine and 2.02 g of triethylamine in 10 ml of anhydrous benzene was added to a solution of 2.51 g of the above described compound, of m.p. 88-89°, in 75 ml of anhydrous benzene, at 10°. The mixture was then stirred for 2 hours. The solution was allowed to stand overnight and filtered; the benzene was distilled off, and the residue was dissolved in dry ethyl acetate and treated with charcoal. Filtration and evaporation of the ethyl acetate left a colorless oil, which crystallized on standing. Recrystallization from ether yielded 1.5 g of material, of m.p. 69-70°. This ethyl ester of N-(diethyleneiminotriazyl)-aminoacetic acid was readily soluble in water, alcohol, ether and ethyl acetate.

Found %: C 50.12; H 6.01; N 32.11. $C_{11}H_{16}O_2N_6$. Calculated %: C 49.99; H 6.10; N 31.80.

6. Methyl ester of N-[2,4-di-(ethyleneimino)-1,3,5-triazyl-6]-D,L-α-aminopropionic acid. a) The initial methyl ester of N-(2,4-dichloro-1,3,5-triazyl-6)-D,L-α-aminopropionic acid was prepared in the same way as the derivative of the ethyl ester of aminoacetic acid (see previous experiment). Colorless crystals were obtained of m.p. 91-94°.

b) The interaction of the above starting material, of m.p. 91-94°, with ethyleneimine was carried out in solution in anhydrous ether at 5° in the presence of triethylamine. After the mixture had stood overnight, it was treated as under 5,c. The oily product was triturated with anhydrous ether to give crystals of m.p. 89-90°. These were dissolved in ethyl acetate and treated with carbon, and the solvent was distilled off to give the methyl ester of N-(diethyleneiminotriazyl)-α-aminopropionic acid, of m.p. 94-95°. This was soluble in water, alcohol, ether, benzene and ethyl acetate.

Found %: C 50.20; H 6.17; N 32.07. $C_{12}H_{18}O_2N_6$. Calculated %: C 50.00; H 6.10; N 31.80.

7. Diethyl ester of N-[2,4-di-(ethyleneimino)-1,3,5-triazyl-6]-D,L-aspartic acid. a) The diethyl ester of N-(2,4-dichoro-1,3,5-triazyl-6)-aspartic acid was obtained by adding a solution of 6.17 g of the ethyl ester of aspartic acid in 30 ml of anhydrous ether, drop by drop with stirring at room temperature, to a solution of 3 g of cyanuric chloride in 100 ml of anhydrous ether. After 1 hour, the precipitate of the hydrochloride of aspartic acid ethyl ester was filtered off, and the ether was distilled off from the filtrate. The yield was 4.77 g of the diethyl ester. M.p. 63-64°.

Found %: N 16.73. $C_{11}H_{14}O_4N_4Cl_2$. Calculated %: N 16.62.

b) A solution of 2.1 g of ethyleneimine was added, drop by drop with stirring, to a solution of 4 g of the diethyl ester of N-(dichloro-1,3,5-triazyl)-aspartic acid in 100 ml of anhydrous ether. Stirring was then continued for 2 hours. The next day, the reaction mixture was treated with charcoal and filtered, and the filtrate was concentrated to a small volume. Colorless crystals deposited after long standing. Yield 3.1 g. The m.p. was 76.5-77.5° after the product had been crystallized from anhydrous ether. The diethyl ester of N-(diethyleneiminotriazyl)-aspartic acid was soluble with difficulty in water, and soluble in alcohol, ether, benzene and ethyl acetate.

Found %: N 23.85. $C_{15}H_{22}O_4N_6$. Calculated %: N 24.00

8. Ethyl ester of N-(2,4-diethyleneimino-1,3,5-triazyl-6)-D,L-α-aminopropionic acid. This was obtained in the same way as the compound described in exp. 7, with the difference that the intermediate – the ester of N-(2,4-dichloro-1,3,5-triazyl-6)-α-aminopropionic acid – was not isolated, but the ethereal solution, containing this substance, was treated with an ethereal solution of ethyleneimine. The corresponding treatment and removal of ether by distillation yielded an oil, which crystallized on standing. M.p. 95-97°. The sample for analysis was recrystallized from anhydrous ether, and melted at 100-101°. The product was soluble in water, alcohol and ether.

Found %: C 51.54; H 6.47; N 30.56. $C_{12}H_{18}O_2N_6$. Calculated %: C 51.77; H 6.55; N 30.20.

9. Benzyl ester of N-(2,4-diethyleneimino-1,3,5-triazyl-6)-D,L- α-aminopropionic acid. The reaction of cyanuric chloride with the benzyl ester of D,L-alanine was carried out in solution in anhydrous benzene; the temperature was maintained at 30° during the time of the reaction. After the solution had been filtered and the benzene distilled off, the ethyl ester of N-(2,4-dichloro-1,3,5-triazyl-6)-D,L-alanine had a m.p. of 125-126°.

The reaction of this substance with ethyleneimine was carried out in anhydrous benzene solution, with cooling. After the solution had been filtered and the benzene distilled off, the residual oil was dissolved in anhydrous ether, and the solution was treated with carbon and the ether distilled off. The colorless crystals remaining had a m.p. of 86-87°. Recrystallization from anhydrous ether gave a product of m.p. 90-91°. The product was insoluble in water, soluble in alcohol, ether and benzene.

Found %: C 59.80; H 5.80. $C_{17}H_{20}O_2N_6$. Calculated %: C 59.98; H 5.92; N 24.7.

10. Methyl ester of N-(2,4-diethyleneimino-1,3,5-triazyl-6)- β-aminopropionic acid. The methyl ester of N-(2,4-dichloro-1,3,5-triazyl-6)-β-aminopropionic acid was prepared as described above for the other compounds of this class. The reaction was carried out in anhydrous benzene solution. Colorless crystals were obtained with a m.p. 102-103°. The reaction of this substance with ethyleneimine was performed in anhydrous ether solution. After the reaction mixture had been filtered and the solvent had been distilled off, a crystalline product was obtained, which, after recrystallization from ethyl acetate, melted at 95-96°; this was soluble in water, alcohol, ether and benzene.

Found %: C 50.15; H 6.09. $C_{12}H_{18}O_2N_6$. Calculated %: C 50.00; H 6.10.

11. Ethyl ester of N-(2,4-diethyleneimino-1,3,5-triazyl-6)- β-phenylaminopropionic acid. a) The ethyl ester of N-(2,4-diethyleneimino-1,3,5-triazyl-6)-β-phenylaminopropionic acid was prepared as described above. The reaction was carried out in anhydrous benzene solution, at room temperature. The crystalline product was recrystallized from anhydrous ether, and then melted at 110-111°.

Found %: C 48.98; H 9.33; N 16.82. $C_{14}H_{14}O_2N_4Cl_2$. Calculated %: C 49.27; H 4.11; N 16.42.

b) The reaction of ethyleneimine with the dichlorotriazine derivative was carried out in anhydrous ether solution, at 8-10°. Filtration, treatment with charcoal, and removal of solvent by distillation yielded an oil, which was treated with a fresh portion of anhydrous ether. On standing, the oil was converted into a colorless amorphous substance, which had no characteristic melting point, since it decomposed on heating.

Found %: C 60.55; H 6.43; N 23.57. $C_{18}H_{22}O_2N_6$. Calculated %: C 60.91; H 6.25; N 23.71.

12. Ethyl ester of N-(2,4-diethyleneimino-1,3,5-triazyl-6)-D,L -α-aminoisovaleric acid. a) The ethyl ester of N-(2,4-dichloro-1,3,5-triazyl-6)-D,L-α-aminoisovaleric acid was prepared from cyanuric chloride and the ethyl ester of aminoisovaleric acid. The reaction was carried out in anhydrous ether at room temperature. After the usual treatment, the oil obtained was redistilled at 0.1 mm. The oil did not solidify.

Found %: C 40.93; H 4.89; N 19.29. $C_{10}H_{14}O_2N_4Cl_2$. Calculated %: C 40.97; H 4.82; N 19.11.

b) The reaction of ethyleneimine with the dichlorotriazine derivative was carried out in anhydrous ether at 8-10°. The reaction mixture was filtered and treated with carbon, and solvent was distilled off until the residual volume was small. Colorless crystals were formed after long standing. These were recrystallized from anhydrous ether to give a product of m.p. 78-79°. This was readily soluble in ether and benzene, with difficulty in water.

Found %: C 55.02; H 7.19. $C_{14}H_{22}O_2N_6$. Calculated %: C 54.88; H 7.24.

13. Diethyl ester of N-(2,4-diethyleneimino-1,3,5-triazyl-6)-D,L-glutamic acid. The diethyl ester of N-(2,4-dichloro-1,3,5-triazyl-6)-D,L-glutamic acid was prepared as described above, the reaction being carried out in anhydrous benzene at room temperature. It was a colorless oil of b.p. 159° at 0.08 mm. The reaction with ethyleneimine was carried out in anhydrous ether. The product was a colorless transparent oil.

Found %: C 52.64; H 6.67; N 23.08. $C_{16}H_{24}O_4N_6$. Calculated %: C 52.73; H 6.64; N 23.06

## SUMMARY

Some 6-substituted 2,4-di-(ethyleneimino)-1,3,5-triazines have been prepared. The substituents were nitrogen containing heterocyclic groups and aliphatic and arylaliphatic amino-acids.

## LITERATURE CITED

[1] Fr. C. Schaefer, J. T. Geoghegan, and D. W. Kaiser, J. Am. Chem. Soc. 77, 5918 (1955).

[2] F. C. Schaefer, J. Am. Chem. Soc. 77, 5922 (1955).

[3] E. Fischer, Ber. 34, 433 (1901).

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# SYNTHESIS OF p-NITROPHENYLHALOGENOMETHYL CARBINOLS

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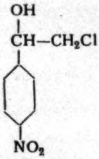
p-Nitrophenylhalogenomethyl carbinols are intermediates for the production of the synthetic antibiotic syntomycin, p-nitrophenylchloromethyl carbinol (I).



(I)

was first synthesized from styrene by V. A. Mikhalev and his co-workers[1]. Styrene chlorohydrin was acetylated, the acetyl derivative was nitrated, and the p-isomer was separated from the mixture of nitro compounds and hydrolyzed to (I).

It appeared of interest to examine the possibility of the direct nitration of styrene chlorohydrin. We found that if the sytrene chlorohydrin was added to the nitration mixture at a temperature below 0°, the product was a mixture of the nitrates of m- and p-nitrophenylchloromethyl carbinols [2]. We were able to separate the ester of the p-nitro derivative by crystallization. To establish its structure, it was oxidized with permanganate to p-nitrobenzoic acid, and it was also prepared from p-nitrophenylchloromethyl carbinol, synthesized by Mikhalev's method. The m-isomer was also isolated, and its structure was established in the same way.

It was necessary to hydrolyze the nitrate in order to obtain p-nitrophenylchloromethyl carbinol. It was found, however, that there is no method given in the literature for hydrolyzing the nitrates of alcohols without also forming considerable quantities of secondary products. In our attempts to hydrolyze the nitrate with aqueous or alcoholic alkali, we obtained much reddish tar and little carbinol. Hydrolysis did not occur when the nitrate was boiled with water and dilute acid. Smooth hydrolysis to the carbinol (with a yield of about 90%) was only achieved by heating the nitrate with a very large excess of concentrated hydrochloric acid. It was found later that it was advantageous to use a mixture of hydrochloric and phosphorous acid, since complete hydrolysis was then achieved with a smaller quantity of acid. It is interesting to note that aqueous phosphorous acid, without hydrochloric acid, did not hydrolyze the nitrate to the carbinol.

Another method of hydrolysis was also found. It is known that alkyl nitrates will nitrate aromatic compounds in the presence of aluminum chloride. It was of interest to investigate the possibility of using this process for hydrolyzing the nitrate. It was found that the nitrate of p-nitrophenylchloromethyl carbinol, on heating with benzene and aluminum chloride, gave an 85% yield of the carbinol with the simultaneous formation of nitrobenzene.

The best yield of carbinol (up to 95%) was obtained by heating the nitrate with 60-65% sulfuric acid in the presence of urea. A more dilute acid gave incomplete hydrolysis.

The nitrate of p-nitrophenylbromomethyl carbinol was obtained by Ernest and Vesely by nitrating styrene dibromide [3]; but these authors did not succeed in hydrolyzing the nitrate. We found that this nitrate could be hydrolyzed by heating with concentrated hydrochloric acid, or preferably with 60% sulfuric acid and urea in precisely the same way as the chloromethyl derivative. p-Nitrophenylchloromethylcarbinol and p-nitrophenylbromomethyl carbinol were oxidized by sodium dichromate, in the normal way, to the corresponding p-nitrochloroacetophenone, of m.p. 91° [4], and p-nitrobromoacetophenone, of m.p. 96-97° [5].

## EXPERIMENTAL

Nitrate of p-nitrophenylchloromethyl carbinol. A mixture of 153 ml of nitric acid (d 1.5) and 306 ml of concentrated sulfuric acid was kept at −2°, and 156.5 g (1 mole) of styrene chlorohydrin was added from a dropping funnel, with vigorous stirring, over a period of 3 hours. The mixture was then stirred for 1 hour at 0°. The product was poured on to ice, filtered off under suction, washed with cold water and with 40 ml of methyl alcohol, and recrystallized from methyl alcohol. Yield 90.6 g (45%). M.p. 78-80°, and 82° after a second recrystallization. The product was readily soluble in benzene, dichloroethane and acetone.

Found %: N 11.16, 11.32. $C_8H_7O_5N_2Cl$. Calculated %: N 11.35.

The mother liquor from the recrystallization was freed from solvent by distillation, and the residue was allowed to stand for two weeks. The nitrate of m-nitrophenylchloromethyl carbinol crystallized out. After two recrystallizations, this had a m.p. of 84° and gave a large m.p. depression when mixed with the nitrate of the p-compound. The m-isomer was readily soluble in dichloroethane, benzene, chloroform and acetone.

Found %: N 11.11, 11.24. $C_8H_7O_5N_2Cl$. Calculated %: N 11.35.

p-Nitrophenylchloromethyl carbinol. a) A mixture of 61.6 g of the nitrate of p-nitrophenylchloromethyl carbinol and 616 ml of concentrated hydrochloric acid was stirred vigorously and heated for 3 hours on a water bath, cooled and filtered. Yield of p-nitrophenylchloromethyl carbinol 45.4 g (90%). M.p. 78-80°.

b) The nitrate (370 g = 1.5 mole) was added gradually to a mixture of 360 g of phosphorous acid, 160 g of concentrated hydrochloric acid and 60 ml of water, and the whole was heated and stirred on a boiling water bath, for 2 hours. Without stopping the stirring, 400 ml of water was added, the mixture was cooled, and the p-nitrophenylchloromethyl carbinol was filtered off. Yield 230 g (92.5%). M.P. 78-79°.

c) Anhydrous aluminum chloride (48 g = 0.36 mole) was added, a little at a time, with stirring, to 197 g (0.8 mole) of the nitrate and 480 ml of dry benzene, at +5°. The mixture was heated slowly on a water bath and boiled for 40 minutes. Then 120 ml of water was added, and the benzene and nitrobenzene formed were distilled off in steam, separated from water and redistilled. The yield of nitrobenzene was 83.8 g (85%). The residue in the reactor was cooled with stirring and the product was filtered off, washed with dilute hydrochloric acid, carefully pressed and stirred with a mixture of 35 ml of petroleum ether and 15 ml of chloroform. The yield of p-nitrophenylchloromethyl carbinol was 137 g (85%). M.p. 78-80°.

d) A mixture of 246.5 g (1 mole) of the nitrate, 60 g (1 mole) of urea and 300 ml of 63% sulfuric acid was heated on a boiling water bath, with stirring, for 2 hours, and then diluted with 500 ml of water and cooled at 10°. The product was filtered off and washed free of acid. Yield 193 g (95%). M.p. 79-81°.

Nitrate of p-nitrophenylbromomethyl carbinol. A mixture of 27 ml of nitric acid (d 1.5) and 60 ml of concentrated sulfuric acid was cooled to −5°, and 25 g of styrene bromohydrin [6] was added, with stirring, over a period of 2 hours, after which stirring was continued for another hour at 0°. The product was poured on to ice, and the solid was filtered off, washed with water and recrystallized from ethyl alcohol. Yield 18.1 g (50%). M.p. 97-98°.

Found %: N 9.46, 9.39. $C_8H_7O_5N_2Br$. Calculated %: N 9.62.

p-Nitrophenylbromomethyl carbinol, of m.p. 84-85° [7], was easily obtained from the nitrate by the method described above: a) by hydrolysis with concentrated hydrochloric acid, in 88% yield, or b) by hydrolysis with 60% sulfuric acid and urea, in 96% yield.

## SUMMARY

A method has been developed for obtaining p-nitrophenylchloromethyl carbinol and p-nitrophenylbromomethyl carbinol by nitration of the corresponding styrene halogenohydrins, and subsequent hydrolysis of the resulting nitrates.

## LITERATURE CITED

[1] V. A. Mikhalev, A. P. Arendaruk, M. L. Galchenko, M. I. Dorokhova, A. M. Zhelokhovtseva, A. I. Ivanov, A. P. Skoldinov, D. D. Smolin, V. A. Skorodumov and N. E. Smolina, Author's Certificate No. 96,868, June 27, 1951.

[2] L. M. Iagupol'skii and A. I. Kiprianov, Author's Certificate No. 99,258, November 18, 1952.

[3] J. Ernest and Z. Vesely, Chem. Listy 47, 746 (1953).

[4] J. Lane and R. Feller, J. Am. Chem. Soc. 73, 4230 (1951).

[5] J. Baker, J. Chem. Soc. 1931, 2420.

[6] J. Read and W. Reid, J. Chem. Soc. 1928, 1487.

[7] C. Guss and H. Mautner, J. Org. Ch. 16, 887 (1951).

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# ABSORPTION SPECTRA AND STRUCTURE OF THE BISULFITE COMPOUND OF ACRIDINE

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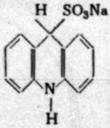
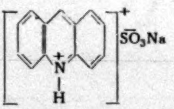
The data in the literature on the structure of the bisulfite compound of acridine is contradictory. Graebe [1] first described two products of the interaction of acridine with sulfurous acid and with sodium bisulfite. One of these, $C_{13}H_9NSO_3HNa$, consisted of colorless crystals readily soluble in water; the other was red, a difficultly soluble substance, of composition $C_{13}H_{10}NSO_3H\ C_{13}H_9N$. Wirth and Lemstedt [2] later assigned to the colorless substance the structure of the sodium salt of dihydroacridine-9-sulfonic acid (I). Drozdov and Cherntsov [3] believed it to be sodium acridinium sulfite (II).



(I)



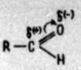
(II)

Grigorovskii [4] considered that there was no real evidence for either of these structures.

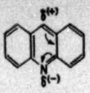
To answer the question of which of these two formulas, (I) or (II), represents the structure of the colorless bisulfite compound of acridine, we compared the absorption spectrum of this substance with those of acridine derivatives having a quinoid configuration of the pyridine ring, such as dihydroacridine and 10-methyl-9-imino acridine, or, for contrast, of the acridinium ion.

The colorless bisulfite compound of acridine was prepared by the method given in the literature [3]. The absorption spectrum was investigated at concentrations from $10^{-3}$ to $10^{-4}$ M in 0.1 N sodium sulfite solution, and at concentrations from $10^{-3}$ to $10^{-5}$ M in water and in ethanol. In the bisulfite and alcohol solutions, an absorption band was observed with a maximum at about 2770 A (Fig. 1, curves 1 and 2). There is a band in this position in the absorption spectra of dihydroacridine [5], p-anthraquinone [6] and 10 methyl-9-iminoacridine [7] (Fig. 1 curves 3-5), all of which are known to have a quinoid structure for the middle ring of the condensed system. This band in the spectrum of the bisulfite compound of acridine was conditionally called the "quinoid" band. Its appearance in the spectrum of this substance could be explained by the addition of a hydrogen atom to the nitrogen in the ring, and of the $NaS_2$ residue to the carbon atom in the 9 position (I). If the $NaS_2$ residue was attached to the 10 position of the acridinium nucleus (II), the absorption curve should resemble that of an acridine salt involving the ring nitrogen; this was not observed in practice (cf. curve 1 of Fig. 1 and curve 1 of Fig. 2).

A similar addition of sodium bisulfite has been noted for other heterocyclic compounds, such as the sulfanilamide derivatives of triazole [8]. A similar addition of sodium bisulfite is well known with compounds containing a carbonyl group. In the present case (acridine) the role of the carbonyl oxygen is fulfilled by the ring nitrogen, which is able to take up an electron. As the result of a shift of electrons in the ring in the direction of the nitrogen, the 9 carbon atom acquires a partial positive charge, and the ring nitrogen a partial negative charge. In this way there is a resemblance between the polarized acridine molecule (IV) and an aldehyde (III)



(III)



(IV)

The bisulfite compound of acridine is relatively unstable. For example, even 2 hours after the preparation of solutions in ethanol or water, in addition to the bands characteristic of the quinoid structure (I), other bands appeared close to those characteristic of the acridinium ion (II). The composite nature of the spectrum of the bisulfite compound could be seen by superimposing the curves (Fig. 1, curve 2 and Fig. 2, curves 2 and 3). This indicated that there was an equilibrium between the sodium salt of dihydroacridine-9-sulfonic acid (I) and the acridinium sulfite (II).

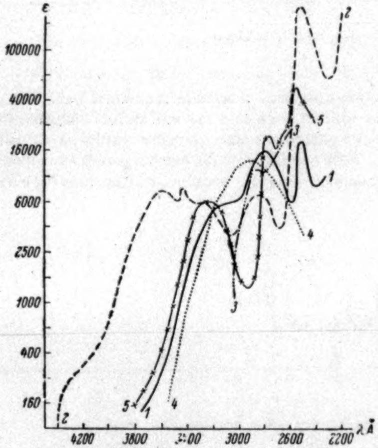


Fig. 1. Absorption spectra. 1) Bisulfite compound of acridine in 0.1 N $Na_2SO_3$, 2) bisulfite compound of acridine in ethanol (immediately after preparation of solution), 3) 10-methyl-9-iminoacridine [7] in methanol (part of curve), 4) dihydroacridine [5] in ethanol, 5) anthraquinone [6] in ethanol.

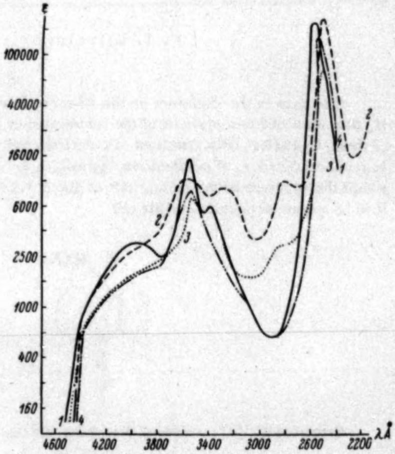


Fig. 2. Absorption spectra. 1) Acridine in a 5 M solution of HCl in ethanol, 2) bisulfite compound of acridine in water (immediately after preparation of solution), 3) bisulfite compound of acridine in water (after solution had stood for 2 hours), 4) bisulfite compound of acridine in water (after solution had stood for 6 days).

$$(I) \underset{Na_2SO_3}{\overset{H_2O}{\rightleftarrows}} (II)$$

With time (after the solution had stood for 6 days), this equilibrium was almost completely displaced towards the side of the acridinium salt (Fig. 2, curve 4, cf. curve 1). The shift of equilibrium towards increase in the acridinium salt was accompanied by a change in the color of the solution; it changed from colorless to yellow, which was brought about by the formation of a positive charge on the ring nitrogen. The reverse process – the change from a colored to a colorless solution – was produced by the addition of sodium sulfite.

## SUMMARY

1) It was established that the absorption spectra of solutions of the bisulfite compound of acridine in sodium sulfite solution, and in solutions in ethanol and water immediately after preparation, had a "quinoid" absorption band. The "quinoid" band of the aqueous solution disappeared after 6 days, and there was a reversion to the spectrum of the acridinium ion.

2. The colorless bisulfite compound of acridine, $C_{13}H_{10}O_3NSNa \cdot 2H_2O$, has been shown to have the structure of the sodium salt of dihydroacridine-9-sulfonic acid, and to change, under the influence of water, to a sulfite (with participation of the ring nitrogen).

## LITERATURE CITED

[1] C. Graebe, Ber. 16, 2830 (1883).

[2] K. Lemstedt and E. Wirth, Ber. 61, 2046 (1928).

[3] N. S. Drozdov and O. M. Cherntsov, J. Gen. Chem. 21, 1710 (1951).*

[4] A. M. Grigorovskii, Prog. Chem. 21, 625 (1952).

[5] E. Blaut and R. Corley, J. Am. Chem. Soc. 69, 763 (1947).

[6] R. Morton and W. Earlam, J. Chem. Soc. 1941, 159.

[7] R. M. Acheson, M. L. Burstall, C. W. Jefford, and B. T. Sanson, J. Chem. Soc. 1954, 3742.

[8] Itaru Inoue and Masaharu Kojima, Ch. A., 463, 925 (1952).

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*Original Russian pagination. See C.B. Translation.

# ABSORPTION SPECTRA AND STRUCTUREOF 2-METHOXY-AMINOACRIDINE-9

V. I. Blizniukov and A. K. Sukhomlinov

The spectrographic investigation of 2-methoxy-9-aminoacridine is of interest because acridine, with a methoxy group in the 2 position, has considerable anti-malarial activity [1]. We have studied the absorption spectra of 2-methoxy-9-aminoacridine in solution in ethanol, dioxane, ether, a M solution of sodium ethylate, ethanol solutions of hydrogen chloride of different concentrations, and in concentrated sulfuric acid, at concentrations from $10^{-3}$ to $10^{-5}$ M.

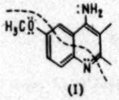
Analysis of the absorption spectra in neutral solvents (Fig. 1, compare curves 1, 2, 5 and 6 with 3 and 4) showed that the "benzenepyridinic" spectrum of acridine was preserved with a 2-methoxy group and a 9-amino group in the acridine ring system. Two absorption bands were observed in these spectra – one, with a maximum at λ 3500 A ($\epsilon$ = 1800), is also present in the spectrum of anthracene, and was therefore called "anthracenic", the other, observed as a shoulder at λ 2950 A[*] ($\epsilon$ = 6000), is characteristic of a para disubstituted benzene in which both the substituents are electron donors [3] (such as p-anisidine), and therefore called "p-anisidinic".

The introduction of a methoxy group into the 2 position of the 9-aminoacridine ring system also resulted in a displacement of the benzenoid bands in the direction of longer wave length, and in the development of a fine structure in the "pyridinic" and long-wave benzenoid bands, of 2-methoxy-9-aminoacridine (Fig. 1, compare curves 1 and 3).

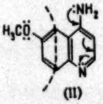
With the solutions in ether and sodium ethylate solution, a "p-aminopyridinic" band was observed with a maximum at λ 2600 A (Fig. 1, curves 5 and 6). The anthracenic band, of $\lambda_{max}$ 3500 A (without the pyridinic band), was also apparent in the spectrum of 9-aminoacridine, when both the ring nitrogen and the amino group had formed salts (Fig. 1, part curve 7). Two other 2-methoxy-9-aminoacridine bands, with maxima at about λ 3350 and 3200 A, were observed in the spectrum of the diacid salt of 9-aminoacridine, and must therefore not be considered as anthracenic bands, but as due to the fine structure of the pyridinic band.

The appearance of two benzenoid bands of the para type in the spectrum of 2-methoxy-9-aminoacridine can be explained as due to the interaction of groups through the $\pi$-electrons of the acridine ring system.

The band with a maximum at λ 2950 A ($\epsilon$ = 6000) is due to electron interaction between the ring nitrogen and the methoxybenzene ring and the methoxy group (I).



(I)



(II)

A similar interaction of ring nitrogen with a benzene ring and a methoxy group has been previously demonstrated by one of us for a number of quinoline derivatives [2].

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[*] The mean point of the curve was taken.

The appearance, in the 2-methoxy-9-aminoacridine spectrum, of an absorption band with a maximum at λ 2600 A is explained by a coupling of the ring nitrogen (electron attracting) with the amino group, through the π-electrons of the pyridine ring (II). The same effect was shown previously for 4-aminopyridine and 4-aminoquinoline [2,4].

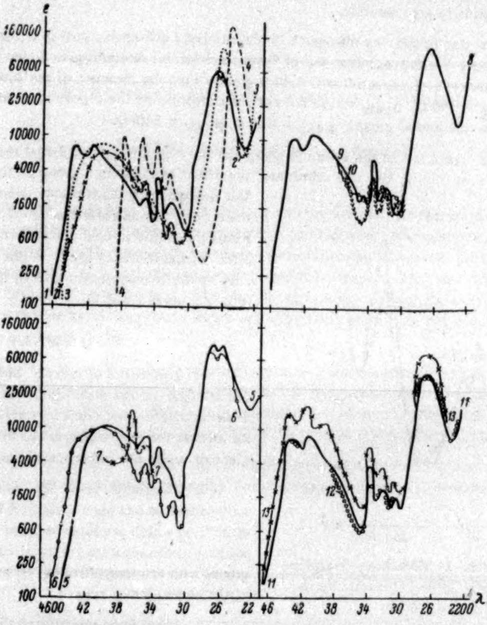

Fig. 1. Absorption spectra. 1) 2-Methoxy-9-aminoacridine in ethanol, 2) 2-methoxy-9-aminoacridine in dioxane, 3) 9-aminoacridine in ethanol, 4) anthracene in hexane, 5) 2-methoxy-9-aminoacridine in ether, 6) 2-methoxy-9-aminoacridine in M sodium ethylate, 7) 9-aminoacridine in 17.5 M $H_2SO_4$ (part of curve), 8) 2-methoxy-9-aminoacridine in ethanolic HCl (ratio 1: 0.2 mole HCl), 9) 2-methoxy-9-aminoacridine in ethanolic HCl (ratio 1: 0.3 mole HCl), 10) 2-methoxy-9-aminoacridine in ethanolic HCl (ratio 1: 0.5 mole HCl), 11) 2-methoxy-9-aminoacridine in ethanolic HCl (ratio 1: 1 mole HCl). 12) 2-methoxy-9-aminoacridine in ethanolic HCl (ratio 1: 100 mole HCl). 13) 2-methoxy-9-aminoacridine in 5 M ethanolic HCl.

In acid ethanolic solutions of hydrogen chloride, even at a ratio of 1: 0.4 mole HCl, the anthracenic band at λ 3500 A and the p-anisidinic shoulder at λ 2950 A were not apparent. The fine structure of the pyridinic band was also better developed, with three maxima at λ 3350, 3320 and 3050 A (Fig. 1, curves 10-13). The same shown for "quinoline-45" [2]. At a ratio of 0.3 mole HCl to 1 mole of 2-methoxy-9-aminoacridine, the third maximum of the fine structure of the pyridinic band appeared at λ 3080 A, and the anthracenic band at λ 3550 A had disappeared, (Fig. 1, curve 9).

Thus in neutral solution, the separate interactions of the ring nitrogen, both with the $\pi$-electrons of the methoxybenzene ring and the methoxy group, and with the $\pi$-electrons of the pyridine ring and the amino group, lead to favorable conditions for electron transfer, in which the ring nitrogen can either attract or give up an electron. In acid media, because the ring nitrogen acquires a positive charge, there is an increase in its capacity to attract an electron from the amino group via the $\pi$-electrons of the pyridine ring. This is why the p-anisidinic and anthracenic bands, with maxima at λ 2950 and 3500 A, disappeared from the spectrum of 2-methoxy-9-aminoacridine in acid solution.

The electron interaction of the ring nitrogen with the methoxy and amino groups is confirmed by the dipole moments of 2-methoxy-9-chloroacridine and of 9-aminoacridine. According to Z. Iu. Kokoshko [5], the dipole moment of 2-methoxy-9-chloroacridine is 0.47 D greater than the moment of the linkage of the methoxy group to the ring: $\mu_{\text{exp}} = 1.70$ D, $\mu_{\text{calc}} = 1.23$ D. For 9-aminoacridine the dipole moment is 0.85 D greater than that calculated from the amino group: $\mu_{\text{exp}} = 4.13$ D, $\mu_{\text{calc}} = 3.28$ D.

The formation of a diacid salt of the 9-amino group and the ring nitrogen of 2-methoxy-9-aminoacridine in concentrated sulfuric acid (Fig. 2, curve 1) eliminated the effect of the amino group on the acridine system. Salt formation by the methoxy group did not occur, since there was no reversion to the spectrum of unsubstituted acridine in concentrated sulfuric acid. The effect of the methoxy group in the 2 position was shown only by the bathochromic shift of the absorption bands (Fig. 2, curves 1 and 2).

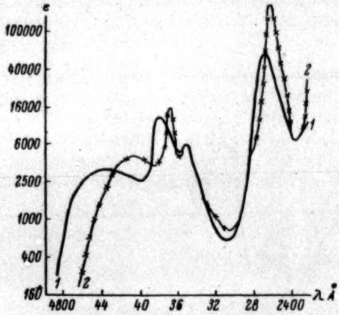

Fig. 2. Absorption spectra. 1) 2-Methoxy-9-aminoacridine in 17.5 M. $H_2SO_4$. 2) 9-aminoacridine in 17.5 M $H_2SO_4$.

## SUMMARY

1. The effect of solvent and of the acidity of the solution on the absorption spectrum of 2-methoxy-9-aminoacridine has been investigated, and it has been shown that the ring nitrogen can attract or give up an electron under the influence of the substituent group.

2. The complicated spectrum of 2-methoxy-9-aminoacridine has been interpreted as "benzene-pyridinic", on which are superimposed three bands corresponding to the separate interactions of the substituent groups with the ring nitrogen, through the $\pi$-electrons of the acridine ring system.

3. It has been established that 2-methoxy-9-aminoacridine forms a diacid salt in concentrated sulfuric acid, involving both the ring nitrogen and the amino group.

In conclusion, we would offer our deepest thanks to A. M. Grigorovskii for his kind gift of 2-methoxy-9-aminoacridine for the spectrographic investigation.

## LITERATURE CITED

[1] O. M. Cherntsov and N. S. Drozdov, J. Gen. Chem. 9, 1435 (1939).

[2] V. I. Blizniukov, Proc. Acad. Sci. USSR 91, 1337 (1953).

[3] N. A. Valiashko, Trans. Kharkov Chem. Tech. Inst. 7, 3 (1943).

[4] B. I. Blizniukov, J. Gen.Chem. 22, 1204 (1952).

[5] Z. Iu. Kokoshko, Thesis "Investigation of the Polarity of Anti-Malarial Derivatives of the Acridine Nucleus," Sverdlovsk (1949).

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Kharkov Pharmaceutical Institute.

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*Original Russian pagination. See. C.B. Translation.

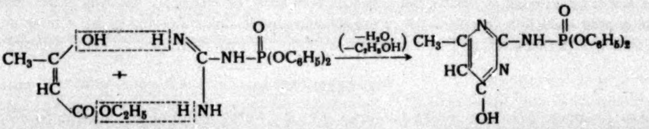
# SYNTHESIS OF PHOSPHORAMIDOPYRIMIDINES

**Iu. P. Shvachkin and M. A. Prokof'ev**

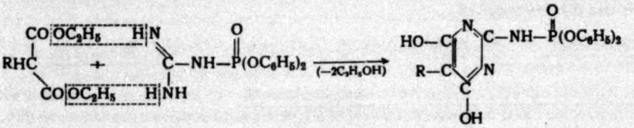
Chemical literature lacks data on phosphorylated aminopyridines. At the same time a study of compounds of this type is of undoubted interest both from theoretical considerations (for example, in connection with the problem of the character of internucleotidic bonds in macromolecules of nucleic acids) and from the practical point of view. Specifically, it is reasonable to expect that the phosphorylated aminopyrimidines may turn out to be analogous in biological activity to the phosphorylated hydroxypyrimidines, among which in recent times some valuable insecticides have been found which act effectively on insects, but which are only weakly toxic to the warmblooded animals [1, 2].

One of the possible paths of synthesis of phosphorylated 2-aminopyrimidines may be the condensation of guanidinophosphoric acids with β-dicarbonyl compounds. In the present paper there are described the syntheses of some 2-phosphoramidopyrimidines, based on the condensation of the diphenyl ester of guanidinophosphoric acid (diphenyl phosphorylguanidine) with compounds of the type of acetoacetic and malonic esters.

Acetoacetic ester condenses with diphenyl phosphorylguanidine on being heated in alcoholic solution in the presence of sodium ethoxide, forming thereby 2-diphenylphosphorylamido-4-hydroxy-6-methylpyrimidine (I) according to the scheme:

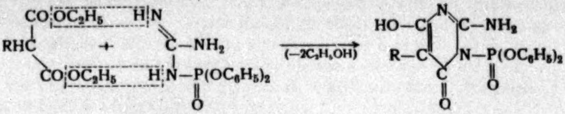


Malonic ester and its homologs condense with diphenyl phosphorylguanidine in analogous circumstances, yielding the corresponding 2-diphenylphosphorylamido-4,6-dihydroxypyrimidines:



(II) $R=H$, (III) $R=CH_3$, (IV) $R=C_2H_5$.

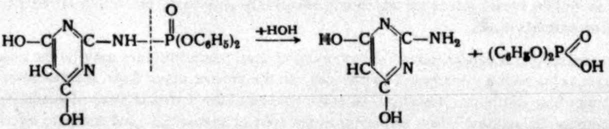
Other directions of condensation, which should lead to the isomeric 2-aminopyrimidines phosphorylated at the nuclear nitrogen, are also theoretically possible, as for example:



However such structures are rather improbable for the compounds prepared by us, since in these synthesized substances the amino nitrogen (by Van Slyke method) is totally lacking, while in the known 2-aminopyrimidines substituted at the nuclear nitrogen the amino group is detectable by this method.

The compounds prepared by us are colorless crystalline substances with rather high melting points. They are readily soluble in the lower alcohols, difficultly soluble in water and aromatic hydrocarbons, and are insoluble in diethyl and petroleum ethers, as well as in acids. In reaction with alkalis (in the cold) they pass into solution readily, binding quantitatively one equivalent of the base. Evidently this is explained by the presence in these compounds of hydroxyl groups which possess acidic properties, similar to those of the phenolic hydroxyl.

A study of the stability to hydrolysis of 4-hydroxy and 4,6-dihydroxyphosphoramidopyrimidines, performed by us with the specimens of compounds (I) and (II), showed that the phosphoramidic bond in these substances is relatively weakly stable, especially in the 4,6-dihydroxy derivatives. Thus, compound (II) is cleaved according to the following scheme in acidic, alkaline and even aqueous hydrolyses:



In this event the resulting 2-amino-4,6-dihydroxypyrimidine decomposes further, as should be expected [3, 4], into malonic acid and guanidine. In cases of acidic and basic hydrolyses there is observed the cleavage of diphenyl hydrogen phosphate which is also not unexpected [5]. In compound (I) the phosphoramidic link is more stable and is not cleaved on boiling the substance with water for one hour. Heating of the compound with normal base or acid leads to a slow cleavage of the phosphoramidic link according to the scheme analogous to that shown above, with formation of 2-amino-4-hydroxy-6-methylpyrimidine and diphenyl hydrogen phosphate.

## EXPERIMENTAL

Diphenyl phosphorylguanidine.* To a solution of 11.2 g (0.192 mole) of guanidine in 50 ml of anhydrous alcohol there was added with energetic stirring and cooling 25.6 g (0.095 mole) of diphenyl chlorophosphonate. The mixture was stirred for thirty minutes longer and was left for five hours at room temperature, after which it was poured into iced water. A colorless oil separated and rapidly crystallized on standing. The crystals were filtered off by suction, washed with ether and dried at 100°. There was obtained 20 g (73%) of diphenyl phosphorylguanidine (diphenyl guanidinophosphate) in the form of colorless crystals; m.p. 118° (from benzene). The literature data [6] give m.p. 118°.

Found %: C 53.25; H 4.83; N 14.77; P. 10.48. $C_{13}H_{14}O_3N_3P$. Calculated %: C 53.61; H 4.84; N 14.43; P 10.63.

2-Diphenylphosphoramido-4-hydroxy-6-methylpyrimidine (I). To the alcoholic solution of sodium ethoxide from 0.58 g (0.025 mole) of sodium and 35 ml of anhydrous alcohol there was added 1.45 g (0.005 mole) of diphenyl phosphorylguanidine. The solution was heated to boiling and, with stirring, it was treated gradually with 3.25 g (0.025 mole) of freshly distilled acetoacetic ester, after which the mixture was refluxed for four hours longer. The alcohol was distilled in vacuum and the residue was dissolved in the least amount of water. The solution was acidified to Congo red with 5% hydrochloric acid. A heavy yellow oil separated and crystallized on standing. The crystals were filtered off, washed with cold water. There was obtained 0.5 g (28%) of colorless crystals; m.p. 182-183° (from n-butyl alcohol).

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*There is a patent on the preparation of diphenyl phosphorylguanidine by the action of guanidine on the mixture of substances formed by the reaction of 2 moles of phenol with 1 mole of phosphorus oxychloride [6]. However, a check showed that the employment of this technique fails to lead to successful synthesis.

Found %: C 56.69; H 4.69; N 11.79; P 8.71. $C_{17}H_{16}O_4N_3P$. Calculated %: C 57.14; H 4.51; N 11.76; P 8. 67.

Amino nitrogen in this compound was undetectable. The substance shows absorption in the ultraviolet region (in solution in ethanol) with: wavelength of maximum of 268 mμ, $\epsilon_{max}$ 6930; $\lambda_{min}$ 253 mμ, $t_{min}$ 5450.

One equivalent of alkali is bound in a reaction with dilute alkali; to a sample of the substance there was added an excess of 0.1 N solution of potassium hydroxide, which was then back-titrated with 0.1 N sulfuric acid in the presence of phenolphthalein.

0.0495 g of substance: 1.48 ml 0.1 N KOH; 0.0370 g of substance: 1.10 ml of 0.1 N KOH. Calculated: 1.39, 1.03 ml of 0.1 N KOH.

2-Diphenylphosphoramido-4,6-dihydroxypyrimidine (II). The compound was prepared analogously to the preceding one from 2.9 g (0.01 mole) of diphenyl phosphorylguanidine, 8 g (0.05 mole) of malonic ester, 1.15 g (0.05 g-atom) of sodium and 40 ml of anhydrous alcohol. The mixture was heated for three hours. The residue after evaporation in vacuum was dissolved in the smallest volume of water. After acidification with hydrochloric acid to pH 1 a heavy yellow oil separated and crystallized rapidly after being rubbed. The crystals were thoroughly washed with absolute ether (three 10-ml portions). There was obtained 1.95 g ( 54%) of colorless crystals with m.p. 159-160° (from chloroform).

Found %: C 53.57; H 3.93; N 11.83; P 8.60. $C_{16}H_{14}O_5N_3P$. Calculated %: C 53.49; H 3.92; N 11.70; P 8.62.

Amino nitrogen was absent in the compound. The substance shows an intense absorption in the ultraviolet region (in solution in ethanol); $\lambda_{max}$ 258 mμ, $\epsilon_{max}$ 19900. One equivalent of base is bound by the substance in reaction with dilute alkali.

2-Diphenylphosphoramido-4,6-dihydroxy-5-ethylpyrimidine (IV). This compound was prepared analogously to the previous one from 2.9 g of diphenyl phosphorylguanidine, 7.52 g of diethyl ester of ethylmalonic acid and 0.92 g of sodium in 40 ml of anhydrous alcohol. Heating lasted for four hours. The residue after evaporation in vacuum was acidified with hydrochloric acid to pH 1. The separated yellowish oil was rubbed with absolute ether. The resulting crystals were filtered off, washed with ether and dried. There was obtained 1.8 g (46.5%) of colorless crystals with m.p. 209-210° (from n-butanol).

Found %: N 10.78, 11.08; P 7.86, 7.74. $C_{18}H_{18}O_5N_3P$. Calculated %: N 10.85; P 7.99.

One equivalent of base is bound by the compound in its reaction with alkali.

Hydrolytic cleavage of 2-diphenylphosphoramido-4,6-dihydroxypyrimidine. a) Aqueous hydrolysis. The compound (II) (0.36 g) was refluxed for one hour with 10 ml of water. Part of the hydrolyzate (5 ml) was acidified with 20% hydrochloric acid to pH 1, extracted with 15 ml of ether, and the ethereal solution was evaporated in vacuum. The residual oil soon crystallized after standing over phosphoric anhydride and potassium hydroxide; the colorless crystals melted at 67-68° and did not give a depressed melting point on mixing with authentic diphenyl hydrogen phosphate [7]. Ultraviolet absorption spectrum of the isolated substance coincides with that of authentic diphenyl hydrogen phosphate (for aqueous solution: $\lambda_{max}$ 262 mμ, $\epsilon_{max}$ 848; $\lambda_{min}$ 231 mμ, $\epsilon_{min}$ 56). On treatment of the compound with ethereal solution of aniline there was obtained a product with m.p. 165°; no depression of melting point was observed with a mixture of the substance with an authentic sample of aniline salt of diphenyl hydrogen phosphate [8]. 2-Amino-4,6-dihydroxypyrimidine and guanidine were detected chromatographically* in the hydrolyzate (the system used was n-butanol – water). Qualitative tests for phenol and phosphoric acid in the hydrolyzate were negative.

b) Alkaline hydrolysis. The compound (II) (0.1808 g) was refluxed with 10 ml of 1 N sodium hydroxide. In samples of the hydrolyzate the content of amino nitrogen was periodically determined by the Van Slyke method.** After 20 minutes an amount of nitrogen was liberated which corresponded to a 97% hydrolysis of the phosphoramidic bond.

After one hour of heating there were detected in the hydrolyzate by the chromatographic method: 2-amino-4,6-dihydroxypyrimidine, guanidine and diphenyl hydrogen phosphate (system n-butanol – acetic acid–water; 1:1:1), as well as phenol (in the form of tribromophenol). After hydrolysis for three hours phosphoric acid was detected (by test with ammonium molybdate).

c) Acid hydrolysis. Compound (II) (0.1808 g) was refluxed with 10 ml of 1 N hydrochloric acid. Amino nitrogen was determined periodically in samples of the hydrolyzate. After sixty minutes an amount of nitrogen was liberated which corresponded to 68.7% hydrolysis of the phosphoramidic bond. 2-Amino-4,6-dihydroxypyrimidine diphenyl hydrogen phosphate and guanidine were detected chromatographically in the hydrolyzate (system of n-butanol which was saturated with water), and there were also detected phenol (as tribromophenol) and phosphoric acid (with formation of ammonium phosphomolybdate).

Hydrolytic cleavage of 2-diphenylphosphoramido-4-hydroxy-6-methylpyrimidine. a) Aqueous hydrolysis. Compound (I) (0.18 g) was refluxed for one hour with 10 ml of water. After cooling of the mixture, the precipitate was filtered off and recrystallized from n-butyl alcohol. Colorless crystals were obtained with m.p. 182-183°, which did not depress the melting point of an authentic and analyzed sample of 2-diphenylphosphoramido-4-hydroxy-6-methylpyrimidine. No other compounds were detected in the hydrolyzate.

b) Alkaline hydrolysis. Compound (I) (0.1811 g) was refluxed for ten minutes with 10 ml of 1 N sodium hydroxide, after which amino nitrogen was determined in a 0.5-ml sample of the hydrolyzate. This yielded 0.490 ml of nitrogen (24°, 749 mm) which corresponded to 62% hydrolysis. 2-Amino-4-hydroxy-6-methylpyrimidine and diphenyl hydrogen phosphate were detected chromatographically in the hydrolyzate (system of butanol–acetic acid – water). Phenol was detected by a qualitative test with bromine water. Phosphoric acid and guanidine were absent in the hydrolyzate.

c) Acid hydrolysis. The compound (0.1815 g) was refluxed for ten minutes with 10 ml of 1 N hydrochloric acid. In a 0.5 ml sample of the hydrolyzate the content of amino nitrogen was determined. There evolved 0.279 ml of nitrogen (22°, 740 mm) which corresponded to a 44% hydrolysis of the phosphoramidic bond. 2-Amino-4-hydroxy-6-methylpyrimidine and diphenyl hydrogen phosphate were detected chromatographically in the hydrolyzate, along with phenol (as tribromophenol). Phosphoric acid was absent in the hydrolyzate.

## SUMMARY

1. A method of synthesis of 2-phosphoramidopyrimidines is suggested, according to which phosphorylated guanidines are condensed with β-dicarbonyl compounds.

2. The following compounds, previously undescribed in the literature, were synthesized: 2-diphenylphosphoramido-4-hydroxy-6-methylpyrimidine; 2-diphenylphosphoramido-4,6-dihydroxypyrimidine; 2-diphenylphosphoramido-4,6-dihydroxy-5-methylpyrimidine; 2-diphenylphosphoramido-4,6-dihydroxy-5-ethylpyrimidine.

3. Hydrolysis of these compounds was studied.

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* Here and later we used ascending chromatograms with development of paper No. 2 of the Leningrad Paper Factory. For development of guanidine we used the color test of Weber [9], while the other compounds were developed by means of ultraviolet absorption.

** The determinations were made in the P. G. Ioanisiani apparatus [10]. The determination required five minutes. A control showed that the amino group of 2-amino-4,6-dihydroxypyrimidine is completely determinable in the five minute period.

## LITERATURE CITED

[1] H. Gysin, Chimia 8, 221 (1954).

[2] K. D. Shvetsova-Shilovskaia, N. N. Mel'nikov and A. F. Grapov, J. Gen. Chem. 26, 808 (1956).*

[3] A. Michael, J. Prakt. Chem. (2) 49, 26 (1894).

[4] W. Traube, Ber. 26, 2551 (1893).

[5] R. H. A. Plimmer and W. J. N. Burch, J. Chem. Soc., 1929, 279.

[6] German Patent 556145 (1932); Chem. Zentr. 1932, II, 2532.

[7] E. Cherbuliez and J. P. Leber, Helv. Chim. Acta 35, 644 (1952).

[8] A. Bernton, Ber. 55, 3361 (1922).

[9] C. I. Weber, J. Biol. Chem. 78, 465 (1928).

[10] P. G. Ioanisiani, Vestnik Moskov. Gos Univ. 1953, 125.

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*Original Russian pagination. See C.B. Translation.

# CHLOROMETHYLATION OF SATURATED α,ω-PHENYLALIPHATIC ACIDS

M. N. Bogdanov

Chloromethylation of saturated α,ω-phenylaliphatic acids is of some interest in connection with research on the synthesis of monomers used to obtain new fibrous polyamides and polyesters. Chromomethylphenylaliphatic acids can be the starting compounds in the synthesis of various α,ω-amino- and α,ω-hydroxycarboxylic acids containing benzene rings on the methylene linkages.

In the present work the chloromethylation of phenylacetic, β-phenylpropionic, γ-phenylbutyric, and δ-phenylvaleric acids of normal structure was carried out; these have not been described as yet in the chemical literature. As in the case of alkylbenzenes [1], this reaction was carried out by passing a stream of hydrogen chloride through a heated mixture of the chloromethylated compound and solution of $ZnCl_2$ in 40% formalin with efficient stirring.

A mixture of ortho and para isomers results from the chloromethylation of phenylaliphatic acids. However, only para isomers were of interest, since the fiber-forming properties were most pronounced in polymers containing para phenyl groups. The saturated p-chloromethylphenylaliphatic acids were separated and purified by crystallizing the reaction products from different solvents. Vacuum distillation was unsuccessful since it was accompanied by polycondensation of the substance with evolution of hydrogen chloride and formation of a yellow viscous tar.

The p-chloromethylphenylacetic, p-chloromethylphenylpropionic, p-chloromethylphenylbutyric, and p-chloromethylphenylvaleric acids obtained were titrated with alkali in a water-alcohol solution; chlorine was quantitatively removed by boiling in an alcoholic $AgNO_3$ solution, and the acids were oxidized to terephthalic acid with 25% nitric acid under pressure (80-90% yield).

## EXPERIMENTAL

Chloromethylation of phenylacetic acid. We used 16.0 g of phenylacetic acid, 5.9 g of $ZnCl_2$, and 55.0 g of formalin. The hydrogen chloride was bubbled for 8 hours at a temperature of 75-80°. The resulting suspension was shaken up with a water - chloroform mixture (100 ml of each). The chloroform solution of the substance was washed twice with water and left to stand in the cold for 24 hours. The first portion of p-chloromethylphenylacetic acid that precipitated was filtered out. The mother liquor was concentrated to a volume of 50 ml and mixed with 50 ml of carbon tetrachloride. The second precipitate was combined with the first and recrystallized from a 20 ml chloroform - 20 ml carbon tetrachloride solution. We obtained 5.2 g of p-chloromethylphenylacetic acid, m.p. 152-153° (24% yield).

Found %: C 58.23, 58.30; H 4.82, 4.93; Cl* 18.72, 18.77. Neutralization equiv. 184.3, 183.2. $C_9H_9O_2Cl$. Calculated %: C 58.53; H 4.91; Cl 19.24. Neutralization equiv. 184.6.

Chloromethylation of β-phenylpropionic acid. We used 20.0 g of β-phenylpropionic acid, 3.3 g of $ZnCl_2$, and 32.0 g of formalin. The hydrogen chloride was bubbled for 6.5 hours at a temperature of 75-80°. The resulting suspension was treated with a 100 ml benzene - 50 ml water mixture. The benzene extract was washed twice with water and the solvent distilled off. The residue was then crystallized from 60 and 80 ml. of carbon tetrachloride. We obtained 7.2 g of p-chloromethylphenylpropionic acid, m.p. 118-119° (27% yield).

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*Chlorine content was determined according to Shulz [2].

Found %: Cl 17.55, 17.51; Neutr. equiv. 197.3, 198.8. $C_{10}H_{11}O_2Cl$. Calculated %: Cl 17.88, Neutr. equiv. 198.6.

Chloromethylation of γ-phenylbutyric acid. We used 46.8 g of γ-phenylbutyric acid, 6.6 g of $ZnCl_2$, and 64.0 g of formalin. The hydrogen chloride was bubbled for 5.5 hours at a temperature of 75-80°. The reaction products were treated with a warm mixture of water (100 ml) and dichloroethane (200 ml). The dichloroethane solution was washed twice with water and allowed to stand in cold for 24 hours. The material that precipitated was carefully dried out and recrystallized from 100 ml of dichloroethane. We obtained 20.0 g of p-chloromethylphenylbutyric acid, m.p. 121-122° (33% yield).

Found %: Cl 16.16, 16.32; Neutr. equiv. 209.7, 210.6. $C_{11}H_{13}O_2Cl$. Calculated %: Cl 16.67; Neutr. equiv. 212.6.

Chloromethylation of δ-phenylvaleric acid. We used 20.0 g of δ-phenylvaleric acid, 2.8 g $ZnCl_2$, and 27.0 g formalin. Hydrogen chloride was bubbled for 5 hours at a temperature of 75-80°. The emulsion formed was treated with a water (50 ml) – carbon tetrachloride (40 ml) mixture. The carbon tetrachloride solution of the substance was washed with water, and the solvent distilled off. The residue was dissolved in a 50 ml benzene – 40 ml ligroin solution. The solution was left standing in the cold for 24 hours. The precipitate was recrystallized from a 10 ml benzene – 30 ml ligroin mixture. We obtained 9.9 g of p-chloromethylphenylvaleric acid, m.p. 76-77° (39% yield).

Found %: Cl 15.51, 15.56; Neutr. equiv. 227.0. $C_{12}H_{15}O_2Cl$. Calculated %: Cl 15.67; Neutr. equiv. 226.7.

## SUMMARY

The chloromethylation reaction of saturated α,ω-phenylaliphatic acids were carried out. The acids obtained (p-chloromethylphenylacetic, p-chloromethylphenylpropionic, p-chloromethylphenylbutyric and p-chloromethylphenylvaleric) have not been previously described in the chemical literature.

## LITERATURE CITED

[1] Org. Reactions, Coll. I. IL, 84 (1948).*

[2] G. Meier, Analysis and Structural Determinations of Organic Substances, Sci.-Tech. Press, Ukrainian SSR, p. 146 (1935).**

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All-Union Scientific Research Institute
of Artificial Fibers

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*Russian translation.

**In Russian.

# ORGANOZINC COMPOUNDS AS CATALYSTS IN THE POLYMERIZATION OF PROPYLENE

G. A. Razuvaev, L. M. Bobinova, and V. S. Emlis

When Natta [1] used Ziegler's catalyst [2] ($Al(C_2H_5)_3 + TiCl_4$) to polymerize propylene, he obtained at first a solid polypropylene. The literature contains information [3] on the use of other group II and III metals (Be, In, Ga, Mg, Cu, Zn) in connection with similar organic reactions; however, no systematic investigation of their catalytic properties has been conducted.

We thought it might be of some interest to study the catalytic activity of organo-zinc compounds (diethyl-, dipropyl-, and diphenylzinc) in propylene polymerization. Diethylzinc with an addition of titanium tetrachloride proved to be active. In the presence of diethylzinc and stannic chloride (or isopropyl sodium) propylene did not polymerize. The effects of reaction temperature, duration, catalyst composition (the molar ratio of $Zn(C_2H_5)_2$ and $TiCl_4$, later denoted as K), and solvent on the polymerization of propylene were investigated. We showed that the best yield of polypropylene is obtained at 110-120° (Table I).

TABLE 1

The Effect of Temperature on the Polymerization of Propylene. Conditions: Solvent – 3 ml of isooctane; K = 1

| $Zn(C_2H_5)_2$ (g) | $TiCl_4$ (g) | $C_3H_6$ (g) | Temperature | Time (in hours) | Yield of polymer (g) | Yield of polymer % |
|---|---|---|---|---|---|---|
| 0.26 | 0.40 | 1.37 | 90—95° | 3 | 0.60 | 43.7 |
| 0.12 | 0.24 | 1.41 | 100—105 | 3 | 0.85 | 60.2 |
| 0.25 | 0.39 | 2.77 | 110—120 | 3 | 2.00 | 73.0 |
| 0.26 | 0.40 | 2.87 | 110—120 | 5 | 2.32 | 83.0 |
| 0.12 | 0.19 | 1.56 | 130—140 | 5 | 0.70 | 43.8 |

When polymerization time was increased from 3 to 5 hours, the increase in polypropylene yield was insignificant (Table I).

It was shown that composition of the catalyst has a great effect on the yield and type of polymer formed. The percent of propylene converted into polymer was largest at the equimolar ratio of $Zn(C_2H_5)_2$ and $TiCl_4$, but the polymer obtained in this case was an oil of varying viscosities. At K = 3 a 30% yield of a hard polymer was obtained (m.p. 150-158°, mol.wt., 10,000-18,000.* If K is further increased the yield of solid polymer noticeably decreases (Table 2).

Heptane and isooctane (2,2,4-trimethylpentane) were tried as solvents in the polymerization of propylene. We determined that in heptane the yield is slightly lower than in isooctane (Table 3).

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* The molecular weight was calculated using the formula $M = \frac{\eta}{2.5 \cdot 10^{-5}}$ [7], where $\eta$, the specific viscosity in tetralin, equals 0.29-0.47.

**TABLE 2**

The Effect of $Zn(C_2H_5)_2$ – $TiCl_4$ Molar Ratio (K) on the Yield of Polypropylene. Conditions: 110-120°, reaction time 3 hours

| $Zn(C_2H_5)_2$ (g) | $TiCl_4$ (g) | K | $C_3H_6$ (g) | Polymer yield (g) | % | The outside appearance of polymer |
|---|---|---|---|---|---|---|
| 0.33 | 0.66 | 0.8 | 1.80 | 1.29 | 72.6 | Oil |
| 0.22 | 0.36 | 0.9 | 1.77 | 1.11 | 62.7 | Oil |
| 0.25 | 0.39 | 1.0 | 2.77 | 2.30 | 83.0 | Oil |
| 0.30 | 0.47 | 1.0 | 2.97 | 1.77 | 59.6 | Viscous oil |
| 0.25 | 0.19 | 2.0 | 0.82 | 0.21 | 25.6 | Semisolid |
| 0.30 | 0.17 | 3.0 | 2.94 | 0.75 | 25.0 | Solid |
| 0.23 | 0.12 | 2.9 | 2.90 | 0.89 | 30.0 | Solid |
| 0.26 | 0.09 | 4.4 | 2.43 | 0.28 | 11.5 | Solid |
| 0.25 | 0.06 | 6.4 | 2.05 | 0.15 | 7.5 | Solid |
| 0.22 | 0.04 | 8.5 | 1.70 | — | — | — |
| 0.30 | 0.0 | — | 1.80 | — | — | — |
| 0 | 0.16 | — | 1.41 | 0.02 | 1.4 | Traces of oil |

**TABLE 3**

The Effect of Solvent on the Polymerization of Propylene. Conditions: 110-120°, reaction time 3 hours

| $Zn(C_2H_5)_2$ (g) | $TiCl_4$ (g) | K | Solvent (in ml) | $C_3H_6$ (g) | Polymer yield g | % | The outside appearance of polymer |
|---|---|---|---|---|---|---|---|
| 0.22 | 0.36 | 0.92 | 0 | 1.77 | 1.11 | 62.7 | Oil |
| 0.21 | 0.29 | 1.15 | Heptane<br>2.04 | 1.32 | 0.74 | 56.0 | Oil |
| 0.26 | 0.28 | 1.40 | 1.96 | 1.34 | 0.44 | 32.8 | Semisolid |
| 0.12 | 0.23 | 0.90 | Isooctane<br>2.13 | 1.41 | 0.85 | 60.2 | Oil |
| 0.26 | 0.30 | 1.50 | 2.15 | 1.37 | 0.50 | 36.2 | Semisold |
| 0.26 | 0.18 | 2.50 | 2.08 | 1.30 | 0.24 | 18.6 | Solid |
| 0.25 | 0.13 | 2.50 | 0.95 | 2.27 | 0.65 | 29.0 | Solid |
| 0.30 | 0.17 | 3.00 | 0.96 | 2.94 | 0.75 | 25.0 | Solid |

When diethylzinc is replaced with dipropyl- and diphenylzinc, the change in the activity of the catalyst, in connection with propylene polymerization, was insignificant. Hence, the nature of the radical shows only small influence on the catalytic ability of the organozinc compound. For the $Zn(C_3H_7)_2 + TiCl_4$ catalysts the effect of molar ratio of the components on yield and type of polymer were investigated (Table 4, 5).

**TABLE 4**

Propylene Polymerization Using $Zn(C_3H_7)_2 + TiCl_4$ atalyst. Conditions: 110-120°, reaction time 5 hours, solvent – 1 ml of isooctane

| $Zn(C_3H_7)_2$ (g) | $TiCl_4$ (g) | K* | $C_3H_6$ (g) | Polymer yield g | % | The outside appearance of polymer |
|---|---|---|---|---|---|---|
| 0.17 | 0.22 | 1.0 | 1.79 | 0.95 | 52.5 | Oil |
| 0.17 | 0.22 | 1.0 | 2.49 | 1.21 | 48.6 | Oil |
| 0.20 | 0.22 | 1.17 | 2.15 | 0.86 | 40.5 | Viscous oil |
| 0.16 | 0.11 | 2.0 | 1.68 | 0.35 | 20.8 | Semisolid |
| 0.17 | 0.07 | 3.0 | 1.82 | 0.27 | 15.2 | Solid |
| 0.17 | 0.05 | 3.7 | 1.83 | 0.20 | 11.3 | Solid |
| 0.32 | 0.04 | 10.0 | 1.25 | — | — | — |

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*K – molar ratio of $Zn(C_3H_7)_2$ and $TiCl_4$.

TABLE 5

Propylene Polymerization Using $Zn(C_6H_5)_2$ + $TiCl_4$ Catalyst. Conditions: 110-120°, reaction time, 5 hours solvent – 1 ml of isooctane

| $Zn(C_6H_5)_2$ (g) | $TiCl_4$ (g) | K* | $C_3H_6$ (g) | Polymer yield |  | The outside appearance of polymer |
|---|---|---|---|---|---|---|
|  |  |  |  | g | % |  |
| 0.20 | 0.17 | 1.0 | 2.50 | 1.63 | 65.0 | Oil |
| 0.24 | 0.11 | 1.9 | 2.70 | 1.67 | 62.3 | Oil |
| 0.22 | 0.11 | 2.0 | 2.45 | 1.22 | 50.0 | Viscous oil |
| 0.25 | 0.07 | 3.0 | 2.50 | 0.54 | 23.0 | Semisolid |
| 0.36 | 0.08 | 3.7 | 2.52 | 0.44 | 17.5 | Solid |
| 0.38 | 0 | — | 2.50 | — | — |  |

## EXPERIMENTAL

Starting Materials. Popylene was obtained by dehydrating isopropyl alcohol over aluminum oxide at 350-400° and carefully purified to remove contaminants. Diethylzinc was obtained from a Zn–Cu alloy and a mixture of bromo and iodoethane [4] (b.p. 30-32° (5 mm)). Dipropylzinc was synthesized in the same fashion as diethylzinc (b.p. 39-40° (9 mm)). The organozinc compounds were used in the form of concentrated isooctane solutions (55-60%). Diphenylzinc was obtained using A. N. Nesmeianov's method of preparation [5], (m.p. 107-109°. The solvents used (chemically pure heptane and isooctane) were in addition dried over sodium.

Polymerization was conducted in molybdenum – glass ampules of about 10 ml capacity. Dry and clean ampules were filled with purified nitrogen. A weighed portion of catalyst and solvent was placed in the ampule. Then a fixed quantity of propylene (1.5-2 g) was condensed into the ampule. A special set-up [6] was used to fill the ampules with nitrogen and condense the propylene. The filled ampules were placed in an electric furnace which was attached to a shaker, and heated to a fixed temperature. At this temperature the contents of the ampules were agitated for 3-5 hours. When polymerization was completed, the ampules were cooled and open. The propylene remaining was evaporated by carefully warming the ampules to room temperature. The contents were poured out into methanol which was then acidified with dilute hydrochloric acid (to destroy the catalyst), and the polymer would precipitate out of solution. The percent of propylene converted into polymer was determined by difference in weight of original and residual propylene. The yield of solid polypropylene was determined directly by weighing the polymer.

## SUMMARY

1. The catalytic activity of diethylzinc with addition of titanium tetrachloride was investigated in connection with the propylene polymerization reaction. The optimum conditions for obtaining a solid polypropylene were determined.

2. It was shown that in the propylene polymerization reaction the activity of catalysts containing dipropyl or diphenylzinc shows only insignificant change from the activity of those containing diethylzinc.

## LITERATURE CITED

[1] G. Natta, La Chimica e L'Industria 38, 2, 121 (1956).

[2] K. Ziegler, Angew. Ch. 67, 541 (1955).

[3] German Patent FRG 883,067, 889,229.

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*K – molar ratio of $Zn(C_6H_5)_2$ and $TiCl_4$.

[4] Synth. Org. Prep., Col. 2, 249 (1949).*

[5] L. G. Makarova and A.N. Nesemelanov Synthetic Methods in the Field of Organometallic Mercury Compounds, Izd. AN SSR, 3rd. ed., p. 125 (1945).*

[6] G. V. Tkachenko, P. M. Khomikovskii and S. S. Medvedev, J. Phys. Chem. 25, 7, 823 (1951).

[7] G. Ciampa, La Chimica e L'Industria 38, 4 (1956).

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*In Russian.

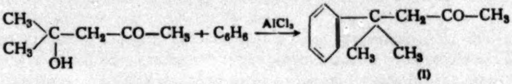
# CONDENSATION OF DIACETONE ALCOHOL WITH BENZENE

## I. P. Labynskii

In recent years I. P. Tsukervanik and co-workers have been conducting a systematic study of condensations between two-functional aliphatic compounds (1,3-butylene chlorohydrin and 1,3-butylene glycol [1], 1,4-pentanediol [2], tertiary diols [3] and aromatic compounds in order to learn the exchange activity of various functional groups. In accordance with the mutual atomic interaction theory [4], a decrease in the interaction of functional groups was detected in the cases where the groups were farther apart. Since they possess theoretical significance, such studies should show new synthetic routes.

We decided to run a condensation of benzene with diacetone alcohol, which has an alcohol group β to the ketonic. Only Niederl's work [5] on condensation of diacetone alcohol with phenol in the presence of $ZnCl_2$ is found in the literature.

One could expect that in diacetone alcohol the alcohol group would react alone or simultaneously with the ketonic group. It appears that when diacetone alcohol is condensed with benzene in the presence of 2 moles of $AlCl_3$, under mild conditions the reaction proceeds at first according to this equation:



(I)

with the formation of 2-phenyl-2-methylpentanone-4 (I) (60.7% yield) and a crystalline substance melting at 127° (II). An increase in temperature or prolongation of the reaction tends to increase the yield of the crystalline product (II).

A separate experiment in which (I) was heated with $AlCl_3$ gave the same product melting at 127° (II). This experiment confirms the secondary origin of substance (II), and consequently shows that condensation proceeds only through the alcohol group.

Some authors [6, 7] obtained the arylketone (I) by condensing mesityl oxide with benzene in the presence of $AlCl_3$. Considering that diacetone alcohol is half as expensive as mesityl oxide, it is more advantageous to obtain the arylketone (I) by our method.

We think, that in analogy the mesityl oxide [7] diacetone alcohol can be condensed with other aromatic hydrocarbons possessing ring hydrogens more active than benzene; in this way various aromatic ketones would be obtained.

## EXPERIMENTAL

From a number of experimental runs only one (that which gave best results) is cited. To a mixture containing 20 g of diacetone alcohol (prepared according to [8]) and 100 ml of benzene, 46 g of $AlCl_3$ was gradually added during 1 hour at 5° with stirring. Subsequently the stirring was continued for 1 hour at 25°. The reaction mixture was decomposed with acidified water, the upper layer separated and dried over $Na_2SO_4$ then distilled at 20 mm. Fractions obtained: 1st 60-127°, 2.1 g; 2nd 128-130°, 21.3 g (60.7%); 3rd 131-200°. 2.9 g (8.7%); residue 0.5 g.

2nd fraction represented 2-phenyl-2-methylpentanone-4 (I).

$n_D^{20}$ 1.5100, $d_4^{20}$ 0.96800, $MR_D$ 54.3; calculated 54.0. Oxime (from alcohol: m.p. 51-52°). Literature data, see [9].

3rd fraction crystallized immediately, m.p. 127° (from benzene).

We heated 5.0 g (I) with 3.8 g of $AlCl_3$ in a petroleum ether solution on a water bath during 2 hours. After the usual treatment 1.7 g of crystalline substance, m.p. 127° (from benzene), were obtained.

This sample when mixed with the substance obtained during condensation did not produce any lowering of the melting point. Substance (II) was not further investigated.

## SUMMARY

It was shown that benzene could be alkylated with diacetone alcohol in the presence of $AlCl_3$ and that 2-phenyl-2-methylpentanone-4 was formed.

## LITERATURE CITED

[1] I. P. Tsukervanik and I. V. Tevent'eva, Proc. Acad. Sci. Uzbek SSR 9, 20 (1950); Author's Certificate No. 88,625 (1950).

[2] I. P. Tsukervanik and N.I. Bogdanova, J. Gen. Chem. 23, 410 (1953).*

[3] L. P. Labunskii and I. P. Tsukervanik, Proc. Acad. Sci. USSR 80, 369 (1951).

[4] V. V. Markovnikov, Data on the Mutual Interaction of Atoms, Kazan (1869).

[5] L. Niederl, J. Am. Chem. Soc. 58, 657 (1936).

[6] A. Hoffmann, J. Am. Chem. Soc. 51, 2542 (1929).

[7] J. Colonge and L. Pichat, Bull. Soc. Chim., 16, 177, 421 (1949).

[8] Synth. Org. Prep., Coll. 1, 184 (1949).**

[9] Dictionary of Org. Compounds 2, 787, 788 (1949).**

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**In Russian.

# SYNTHESIS OF ORGANOPHOSPHORUS COMPOUNDS FROM HYDROCARBONS AND THEIR DERIVATIVES

## VIII. A STUDY OF OXIDATION OF PHOSPHORUS TRICHLORIDE BY OXYGEN

M. K. Baranaev, Iu. M. Zinov'ev, T. K. Skripach
and L. Z. Soborovskii

Oxidative chlorophosphonation of hydrocarbons and their derivatives is a conjugated reaction as the result of which compounds containing a phosphorus – carbon bond preformed. Simultaneously there occurs the oxidation of the phosphonating agent used, $XPCl_2$ (X = chlorine, alkyl or aryl residues, alkoxy, dialkylamino or other monovalent organic groups) to the corresponding compounds of quinquevalent phosphorus: $RH + 2XPCl_2 + O_2 \rightarrow RP(O)XCl + XP(O)Cl_2 + HCl$.

Oxidative chlorophosphonation is applicable to various classes of hydrocarbons and their derivatives [1-6]. In all cases the process of formation of a phosphorus-carbon begins evidently with oxidation of phosphorus trichloride.

Few studies are extant in which oxidation of phosphorus trichloride by oxygen has been studied. There are only the indications by Remsen of the possibility of oxidation of phosphorus trichloride by ozonized oxygen [7]* and a patent with a description of "burning" at 150° of a gaseous mixture of phosphorus trichloride and oxygen taken in 2:1 molar proportion [9].

Our observations show that oxidations of both the phosphorus trichloride itself and of the compounds formed from it and corresponding to the formula $XPCl_2$ are readily realized by the simple passage of gaseous oxygen or air through the appropriate reactants.

Previously a supposition was expressed about the radical character of both the oxidative chlorophosphonation and the oxidation of pure phosphorus trichloride [10]. According to this supposition the primary act in the oxidation of phosphorus trichloride is the addition of a molecule of oxygen to phosphorus trichloride. The resulting adduct may be regarded as a biradical ($Cl_3\dot{P}O\dot{O}$) or as a bipolar ion ($Cl_3\overset{+}{P}O\overset{-}{O}$): $PCl_3 + O_2 \rightarrow Cl_3\dot{P}O\dot{O}$.

In the case of oxidation of pure phosphorus trichloride this adduct reacts immediately with a second molecule of phosphorus trichloride and forms phosphorus oxychloride : $Cl_3\dot{P}O\dot{O} + PCl_3 \rightarrow 2POCl_3$.

Thus all of the phosphorus trichloride is gradually converted into phosphorus oxychloride, i.e. the process is completed. However if a hydrocarbon (RH) is present in the reaction mixture, the possibility arises of involvement of the latter in the reaction.

Biradical $Cl_3\dot{P}O\dot{O}$ colliding with a molecule RH forms an organic radical R· and a radical OH: $Cl_3\dot{P}O\dot{O} + RH \rightarrow POCl_3 + R\cdot + \dot{O}H$. These radicals may account for the origin of the phosphorous-carbon bond and may lead to the formation of chlorides of the corresponding alkylphosphonic acids.

Oxidative chlorophosphonation may be regarded, therefore, as an example of conjugated oxidation which proceeds according to the scheme which resembles that proposed by N.A. Shilov [11] for processes of autooxidation.

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* Evidently this paper served as the basis for Nekrasov's assertion about the difficulty of oxidation of phosphorus trichloride by oxygen which allegedly requires the presence of ozone or the use of a catalyst [8].

According to Shilov's concepts, a conjugation of reactions is possible only in those cases in which there exists an intermediate substance which connects the primary and the secondary processes. At the same time a characteristic peculiarity of conjugated reactions (in contrast to catalytic reactions) is their low order of dependence on the conditions under which the interaction of the reactants takes place.

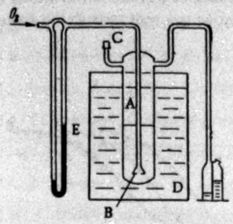

Fig. 1. Scheme of apparatus.

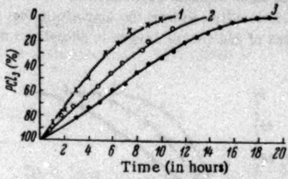

Fig. 2. Oxidation of $PCl_3$ at constant temperature (25°) with varying stirring. Volume of $PCl_3$ (in ml.): 1) 25, 2) 50, 3) 60.

For a better understanding of the complex process of formation of the phosphorus – carbon bond it appeared reasonable to study the reaction of oxidation of phosphorus trichloride in more detail.

It is shown in the present work that the above-described scheme of oxidative chlorophosphonation agrees well with facts which are observed during the oxidation of phosphorus trichloride by gaseous oxygen under various conditions. A study of the kinetics of oxidation of phosphorus trichloride was made not only with pure $PCl_3$, but also in the presence of iodine and for a mixture with cyclohexane. The study of oxidation of phosphorus trichloride by oxygen in the presence of iodine was undertaken since it had been noted previously that in such a case the oxidative phosphonation is hindered (an analogous effect is caused by ferric chloride, nitrobenzene and some other reagents) [1]. Introduction of cyclohexane into the reaction should permit one to observe the process under the conditions which lead to the formation of the C–P bond.

Oxidation of phosphorus trichloride was run in vessel A (Fig. 1), provided with a gas inlet tube with a porous glass plate B and opening C, closed by a ground-in stopper. Vessel A is placed in a thermostat D, which assures the temperature level desired for the experiment with an accuracy of ± 0.1°. Into vessel A there was placed a known volume of freshly-distilled phosphorus trichloride and oxygen was passed in, the rate of flow of which was controlled by the flowmeter E. The content of trivalent phosphorus in phosphorus trichloride was determined before the start of the experiment. After predetermined time intervals, samples were taken in which the content of trivalent phosphorus was determined (iodometrically). The rate of passage of oxygen was constant in all experiments (0.05 liter per minute). Oxidation was run at various temperatures (0, 25 and 40°). In order to make observation on the effects of stirring on the process possible, various amounts of phosphorus trichloride (25, 50 and 60 ml) were used for the reaction. In the presence of additives (cyclohexane and iodine) the oxidation was realized in all cases at 25° while the liquid volume was held at 25 ml. The experimental results are shown in Figs. 2-4.

Curves which show the degree of oxidation of phosphorus trichloride with time indicate that the process proceeds at a constant rate which changes only with conditions of agitation until some 60-70% of the reactant taken had been oxidized. The rate of oxidation in this period is greater, the better are the conditions of agitation (Fig. 2). Thus, the reaction of oxidation of phosphorus trichloride by gaseous oxygen is a heterogeneous process, the rate of which is determined, at least in the initial stage, by the rate of dissolution of oxygen. All factors which aid the acceleration of absorption of oxygen by the liquid phase should accelerate the oxidation.

Increased rate of oxidation in the presence of cyclohexane may be explained also by the greater rate of absorption of oxygen from the gaseous phase under these conditions.

With decrease of the concentration of phosphorus trichloride in the liquid phase from the initial value to 40-30%, the rate of oxidation declines. During this period, the rate of dissolution of oxygen probably does not change materially and a gradual accumulation of it in the liquid takes place. In this stage the course of the process of oxidation is determined not only by the rate of passage of oxygen through the interface of gas and liquid, but also by the rate of its reaction with phosphorus trichloride in the homogeneous liquid phase. Thus, for example, the rates of oxidation of phosphorus trichloride with added cyclohexane and without the latter are almost the same at equal concentrations of the unoxidized material (less than 30% of the initial value) (Fig. 3). This additionally confirms the supposition that the process of phosphonation proceeds through the formation of a product of addition of oxygen to phosphorus trichloride.

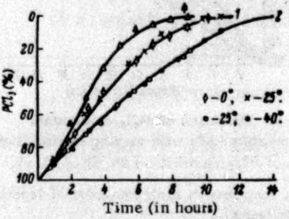

Fig. 3. Oxidation of $PCl_3$ at various temperatures. Volume of $PCl_3$: 1) 25 ml, 2) 50 ml, 4) $PCl_3$ + 25 ml $C_6H_{12}$ at 25°.

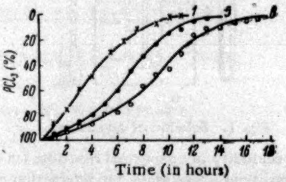

Fig. 4. Oxidation of $PCl_3$ in the presence of iodine (25 ml, 25°). 1) Without iodine, 5) 0.005% iodine, 6) 0.01% iodine.

Insignificant (0.05-0.02%) additions of iodine greatly hinder the oxidation. The solubility and the rate of absorption of oxygen evidently cannot be changed significantly as the result of addition of such small amounts of iodine. Consequently, in this case the slowest process is the homogeneous reaction of oxidation of phosphorus trichloride by the dissolved oxygen. The S-shaped course of the curves of oxidation of phosphorus trichloride with addition of 0.01 and 0.005% of iodine indicates that iodine, as a negative catalyst, is gradually consumed – leached out from the solution by the excess oxygen or is neutralized in the process of the reaction (Fig. 4).

In agreement with the supposition regarding the heterogeneous nature of the process of oxidation of pure phosphorus trichloride, one may expect some insignificant changes of its rate with alteration of temperature. This supposition is completely confirmed by experiment. The rate of reaction at 0, 25 and 40° is practically the same (Fig. 3).

However, the rate of oxidation is independent of temperature not only in the initial phase, but also after the rate of the whole process begins to depend on the amount of unreacted phosphorus trichloride. Therefore, the rate of the homogeneous reaction of oxidation of phosphorus trichloride by the dissolved oxygen is also practically independent of temperature. This shows that the energy of activation of oxidation of phosphorus trichloride is very small and the process, evidently, has the free radical character, proceeding by the scheme shown above, with intermediate formation of the radical $Cl_3\dot{P}O\dot{O}$.

## SUMMARY

1. The initial stage of oxidation of phosphorus trichloride by gaseous oxygen is a heterogeneous process, the rate of which is determined by the rate of dissolution of oxygen.

2. The rate of oxidation of phosphorus trichloride by gaseous oxygen is practically independent of temperature both in the beginning and at the end of the process.

3. The activation energy of oxidation of phosphorus trichloride by oxygen is very small, which agrees with the supposition about the free radical character of this process.

## LITERATURE CITED

[1] L. Z. Soborovskii, Iu. M. Zinov'ev and M. A. Englin, Doklady Akad. Nauk SSSR 67, 293 (1949).

[2] L. Z. Soborovskii, Iu. M. Zinov'ev and L. I. Muler, J. Gen. Chem. 24, 380 (1954).*

---

*Original Russian pagination. See C.B. Translation.

[3] L. Z. Soborovskii and Iu. M. Zinov'ev, J. Gen. Chem. 24, 516 (1954).*

[4] L. Z. Soborovskii, Iu. M. Zinov'ev and L. I. Muler, Doklady Akad. Nauk SSSR 109, 98 (1956).*

[5] Iu. M. Zinov'ev and L. Z. Soborovskii, J. Gen. Chem. 26, 3030 (1956).*

[6] Iu. M. Zinov'ev, V. N. Kulakova and L. Z. Soborovskii, J. Gen. Chem. 28, 1551 (1958).*

[7] J. Remsen, Am. J. Sci. 11, 365 (1876).

[8] B. V. Nekrasov, Course in general chemistry, p. 397 (1954).**

[9] Jap. Pat. 4351 (1950) [Chem. Abstr. 46, 10560 (1952)].

[10] L. Z Soborovskii, Iu. M. Zinov'ev and M. A. Englin, Doklady Akad. Nauk SSSR 73, 333 (1950).

[11] N. A. Shilov, Concerning conjugated oxidation reactions (1905).**

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*Original Russian pagination. See C.B. Translation.

** In Russian.

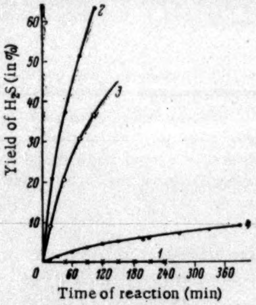
# REACTIONS OF FREE RADICALS IN SOLUTION

## XIV. FORMATION OF FREE RADICALS IN DECOMPOSITION OF HYDROGEN DISULFIDE AND THEIR REACTIONS WITH $\alpha$- AND $\beta$-OLEFINS

E. I. Tiniakova, E. K. Khrennikova and B. A. Dolgoplosk

A series of papers devoted to the study of reactivity of free radicals with $\alpha$- and $\beta$-olefins have been appearing recently. Reactions of alkyl free radicals with $\alpha$-olefins proceed mainly in the direction of their addition to the double bonds with a corresponding decrease of the role of reactions of hydrogen cleavage [1]. In case of $\beta$-olefins the predominant reaction of the methyl radical is the cleavage of a hydrogen atom with formation of methane [14]. Analogous data have been obtained also for the radical with the reactive center on the nitrogen atom $(CH_3)_2N\cdot$ [2]. Reactions of free radicals of type $RO\cdot$ and $RO_2\cdot$ with various olefins mainly proceed in the direction of cleavage of a hydrogen atom with formation of the corresponding alcohols and hydroperoxides [3].

The present communication is devoted to the study of reactivity of $\cdot SH$ radicals with $\alpha$- and $\beta$-olefins; this study has a real interest in its connection with their role in the process of vulcanization with sulfur [4].



Decomposition of hydrogen disulfide in ethylbenzene solution at 70° in quartz ampul in nitrogen atmosphere ($H_2S$ concentration in solution is 2 weight %). 1) in NO atmosphere, 2) freshly prepared $H_2S_2$, 3) $H_2S_2$ treated with HCl for 3 hours, 4) $H_2S_2$ stored under HCl for 3 weeks.

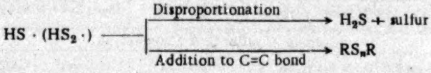
As the source of $\cdot SH$ radicals, we used hydrogen disulfide which as is known, decomposes readily with formation as end products of hydrogen sulfide and sulfur. The decomposition of hydrogen disulfide proceeds particularly intensively in the presence of alkalis, amines and other compounds of basic character [5]. The reaction is retarded in the presence of dilute mineral acids, especially hydrochloric, as a result of which fact hydrogen disulfide is generally stored in an atmosphere of dry hydrogen chloride. In such organic solvents as xylene, toluene, ethylbenzene, isopropylbenzene, etc., the decomposition also proceeds with liberation of equivalent amounts of hydrogen sulfide and sulfur; in this case the decomposition occurs with considerably greater speed in ampuls made of ordinary glass than in quartz vessels [4]. The rate of decomposition of hydrogen disulfide decreases with increased duration of the time of its storage in the atmosphere of hydrogen chloride (see figure). In a solution of rubber in the same solvents the decomposition proceeds without an observable liberation of hydrogen sulfide, while the effect of vulcanization (gel formation) is seen [4].

Evidently, the decomposition of hydrogen disulfide, analogously to that of hydrogen peroxide, proceeds by a chain mechanism through the stage of $\cdot SH$ and $\cdot S_2H$ radicals; here the sulfhydryl radicals, in contrast to the majority of aliphatic and hetero-radicals, do not participate in the reaction with the solvent. The absence of reaction $\cdot SH + AH \rightarrow H_2S + A\cdot$ (where AH is the solvent) indicates the equimolar ratio of amounts of sulfur and hydrogen sulfide formed in the decomposition of hydrogen disulfide. The formation of equivalent amounts of sulfur and hydrogen sulfide on thermal decomposition of hydrogen disulfide may be connected only with reactions of disproportionation and chain transfer:

$$\begin{gathered} HSSH \rightarrow HS\cdot + \cdot SH \\ HS\cdot + HSSH \rightarrow H_2S + HS_2\cdot \\ HS_2\cdot + HS\cdot \rightarrow H_2S + S_2 \text{ ( or } H_2S_2 + S) \\ HS\cdot + HS\cdot \rightarrow H_2S + S \end{gathered}$$

The radical character of the reaction is also confirmed by the data obtained by us on the composition of hydrogen disulfide in the presence of a free-radical acceptor – nitrogen oxide (figure). On heating hydrogen disulfide in ethylbenzene solution at 70° under conditions of a continuous passage of gaseous NO through the solution, the decomposition proceeds without liberation of hydrogen sulfide. It was shown previously that hydrogen sulfide does not react with NO under the indicated conditions for the reaction.

In decomposition of hydrogen disulfide in the absence of olefins there may develop two competing directions of reaction:



We studied the decomposition of hydrogen disulfide in various olefins containing terminal and internal double bonds.

The relative reactivity of hydrogen disulfide and olefins and the character of the reactions which occur were evaluated by the amount of hydrogen sulfide liberated and by the composition of the resulting addition products. The results are shown in Tables 1 and 2. If follows from the data in Table 1 that during the decomposition of hydrogen disulfide in olefins containing a vinyl double-bond (α-pentene styrene, isoprene), the reaction of formation of hydrogen sulfide is almost completely repressed. In cases of olefins with an internal double bond (β-pentene, cyclohexene) which are weaker acceptors of free radicals, the decomposition of hydrogen disulfide is accompanied by formation of hydrogen sulfide, the amount of which, however, is much smaller than in decomposition in inert solvent.

TABLE 1

Yield of $H_2S$ in Decomposition of Hydrogen Disulfide in Ethylbenzene and Olefins

| Solvent | Temperature | Yield of $H_2S$ (in % of theoretical)* |
|---|---|---|
| Ethylbenzene | 70° | 97-98 |
| Isoprene | 70 | 2.0 |
| Styrene | 70 | 5.0 |
| α-Pentene | 50 | 9.0-10.8 |
| α-Pentene | 130 | 5.2 |
| β-Pentene | 50 | 42-48 |
| Cyclohexene | 50 | 59.2-62.0 |

The products of reaction of hydrogen disulfide with α- and β-pentenes, as well as cyclohexene, were isolated and characterized as models of the structure of the cis-1,4 link of polybutadiene (Table 2). From data in this table it follows that in decomposition of hydrogen disulfide in α-pentene the main product of the reaction is a monosulfide, the yield of which is 30-40%. Along with the monosulfide there were isolated and characterized the diamyldisulfide and diamyltetrasulfides,as well. The total yield of isolated mono-, di- and tetrasulfides was about 75%. In β-olefins (β-pentene, cyclohexene), the reaction also leads to the formation of sulfides (mono-, di- and tetra-), the total yield of which, however, is considerably below the yield of these products in the decomposition run in α-olefins, owing to the parallelly-running course of the process of formation of hydrogen sulfide. The summary yield of isolated sulfides and hydrogen sulfide after the reaction in β-pentene was 58%, and after the reaction in cyclohexene it was about 50%. The higher yield of alkyl sulfides in the case of decomposition of hydrogen disulfide in α-pentene corresponds to its greater reactivity in reactions with free radicals. The yields of various alkyl sulfides after decomposition of hydrogen disulfide in α- and β-olefins were rather close after recalculation to the amount of $H_2S_2$ which[*] had added, this fact indicating the similar mechanism of their formation.

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*Theoretical yield was taken as the amount of $H_2S$ formed by equation: $H_2S_2 \rightarrow H_2S + S$.

TABLE 2

Composition of Products of the Reaction of Hydrogen Disulfide with Olefins (Temperature 50°, duration of reaction 15 hours)

| Reaction product | α-Pentene(conc.of $H_2S_2$ 1.08 mole/liter) | | β-Pentene(conc. of $H_2S_2$ 1.18 mole/liter) | | Cyclohexene(conc. of $H_2S_2$ 1.01 mole/liter) | |
|---|---|---|---|---|---|---|
| | Content of sulfur in the product, % | | | | | |
| | Calc. on sulfur introduced as $H_2S_2$ | Calc. as sulfur in added $H_2S_2$ | Calc. as sulfur introduced as $H_2S_2$ | Calc. as sulfur in added $H_2S_2$ | Calc. on sulfur introduced as $H_2S_2$ | Calc. on sulfur in added $H_2S_2$ |
| $H_2S$ | 4—5 | — | 21 | — | 29—31 | — |
| RSH | 0.5—1 | 0.55 | 0 | — | 3.2 | 8.0 |
| $R_2S$ | 31—39 | 34.5 | 14.9 | 25.7 | 7.75 | 9.5 |
| $R_2S_2$ | 10 | 11.1 | 3.0 | 5.2 | 7.42 | 18.5 |
| $R_2S_4$ | 25 | 27.8 | 18.7 | 32.4 | — | — |
| $R_2S_n$ + S | 18 | — | 30.9[**] | — | 42.4 | — |

The formation of sulfides in the decomposition of hydrogen disulfide in olefins may be connected only with the participation in the reactions of free radicals.

The most probable mechanism of the reaction is shown in the scheme below.[***]

a) Initiation stage.

$$HSSH \longrightarrow 2 \cdot SH.$$

b) Formation of monosulfide.

$$ACH{=}CH_2 + \cdot SH \rightarrow A\underset{\cdot}{C}H{-}CH_2SH \xrightarrow{HSSH} ACH_2{-}CH_2SH + HS_2 \cdot \rightarrow$$
$$\xrightarrow{R\cdot} RH + ACH_2{-}CH_2S \cdot \xrightarrow{ACH=CH_2} ACH_2{-}CH_2S{-}CH_2{-}\underset{\cdot}{C}HA \xrightarrow{HSSH}$$
$$\longrightarrow ACH_2{-}CH_2{-}S{-}CH_2{-}CH_2A.$$

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[*] Amount of $H_2S$ which had added was determined by the difference between the introduced hydrogen disulfide and that consumed in formation of sulfur and hydrogen sulfide, which always formed in the reaction in equivalent amounts.

[**] 15.6% of crystalline sulfur, with m.p. 114°, was isolated from the mixture.

[***] Under the conditions of the reaction, prepared hydrogen sulfide does not add to olefins.

c) Formation of disulfides:

1) Recombination of radicals.

$$2ACH_2{-}CH_2S\cdot \longrightarrow ACH_2{-}CH_2S{-}SCH_2{-}CH_2A,$$

$$2)\ ACH{=}CH_2 + \cdot S_2H \rightarrow A\underset{\cdot}{C}HCH_2SSH \xrightarrow{HSSH} ACH_2CH_2SSH \xrightarrow{R\cdot}$$
$$\longrightarrow ACH_2CH_2SS\cdot \xrightarrow{ACH=CH_2} ACH_2{-}CH_2{-}SS{-}CH_2{-}\underset{\cdot}{C}HA \xrightarrow{HSSH}$$
$$\longrightarrow ACH_2CH_2{-}S{-}S{-}CH_2{-}CH_2A.$$

d) Formation of tetrasulfides.

$$2ACH_2CH_2SS\cdot \longrightarrow ACH_2CH_2{-}SSSS{-}CH_2CH_2A \text{ etc.}$$

## EXPERIMENTAL

Hydrogen disulfide was prepared by fractional distillation of hydrogen polysulfide in vacuum [6]. B.p. 75°, $d_4^{15}$ 1.715. In all cases freshly prepared hydrogen disulfide was used for the study of the reaction in olefins.

α-Pentene was prepared from ethyl bromide and allyl bromide [7]. B.p. 30°, $n_D^{20}$ 1.3720.

β-Pentene was prepared by dehydration of secondary amyl alcohol [8]. B.p. 35.5° at 736 mm, $n_D^{20}$ 1.3790.

Cyclohexene was prepared by dehydration of cyclohexanol [9]. B.p. 83.5°, $n_D^{20}$ 1.4453.

The olefins were thoroughly dried and were distilled through a column directly before the experiment.

The reaction of hydrogen disulfide with olefins was run in sealed ampuls in a nitrogen atmosphere. For protection of $H_2S_2$ from a premature decomposition the ampuls were preliminarily kept for several hours in the atmosphere of dry gaseous hydrogen chloride. After this, the ampuls were pumped out several times with an oil pump, were filled with dry nitrogen, after which the solution of $H_2S_2$ was introduced countercurrent to the stream of nitrogen, the solution having been prepared directly before the experiment in a quartz flask.

The sealed ampuls were heated in a thermostat at 50° for 15 hours. After completion of the reaction, the ampuls were cooled to −70°, were opened, connected to an absorption system for taking up hydrogen sulfide (cadmium chloride solution), and a stream of nitrogen was passed through the solution at 0° for the removal of hydrogen sulfide, which was then determined iodometrically [10].

Individual samples of the solution, after the removal of $H_2S$ from it, were analyzed for the content of mercaptan and for the completeness of decomposition of $H_2S_2$. For determination of completeness of decomposition of $H_2S_2$, several milliliters of the solution were shaken with 10% solution of cadmium chloride, with which $H_2S_2$ forms a precipitate of $CdS_2$. In all experiments $CdS_2$ was absent, which fact indicates the complete decomposition of hydrogen disulfide.

The solvent was distilled from the reaction mixture at atmospheric pressure, and the residue was fractionated in vacuum. The resulting crude sulfides were again distilled. Elemental composition, index of refraction and density at 15°, molecular weight by cryoscopic method, functional groups (SH, S, S-S) [12] and unsaturation by means of IBr solution in carbon tetrachloride [11], were determined for the reaction products after their isolation in the pure state. The disulfides were reduced with zinc dust in acetic acid and the resulting mercaptan was determined argentometrically [12]. The polysulfides were treated by boiling with sodium sulfite for the removal of elemental and polysulfide sulfur [13]. The disulfide formed thereby was determined argentometrically [12]. The monosulfide sulfur was determined by bromination [12].

Reaction of $H_2S_2$ with α-pentene. There was taken 3.05 g of $H_2S_2$ in 50 ml of α-pentene. There was isolated: a) $H_2S$ 0.19 g (5.4% of the theoretical amount*).

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*In all cases the theoretical amount was taken as the amount of product ($H_2S$, mono-, di- and tetrasulfide) which could form from all sulfur contained in the $H_2S_2$ taken.

b) Diamyl monosulfide 4.78 g. (31.0%).

B.p. 86-87° at 12-13 mm, $d_4^{15}$ 0.8446, $n_D^{15}$ 1.4572.

Found %: C 68.44; H 12.72; S 18.37. M 171. Iodine number 0; content of monosulfide sulfur 10%. $(C_5H_{11})_2S$. Calculated %: C 68.96; H 12.64; S 18.39. M 174.

c) Diamyl disulfide 0.94 g (11.8%).

B.p. 68-75° at 1 mm, $d_4^{15}$ 0.9381, $n_D^{15}$ 1.5038.

Found %: C 58.20; H 10.58; S 30.44. M 198, 201; Iodine number 0; content of disulfide sulfur 102%. $(C_5H_{11})_2S_2$. Calculated %: C 58.25; H 10.68; S 31.07. M 206.

d) Diamyl tetrasulfide 1.7 g (25%).

B.p. 100-107° at 1 mm, $n_D^{20}$ 1.5285.

Found %: C 43.84; H 8.92; S 47.25. M 268; Iodine number 0. $(C_5H_{11})_2S$. Calculated %: C 44.44; H 8.15; S 47.40. M 270.

e) Residue after distillation was a mixture of sulfur with a small amount of the tetrasulfide and possibly still higher polysulfides.

Reaction of $H_2S_2$ with β-pentene. There was used 5.6 g of $H_2S_2$ in 50 ml of β-pentene. There were isolated: a) $H_2S$ 1.17 g (21%).

b) Diamyl monosulfide 4.26 g (14.9%).

B.p. 79° at 10 mm, $d_4^{15}$ 0.8426, $n_D^{15}$ 1.4568.

Found %: C 69.38; H 12.61; S 18.68. M 173; iodine number 0; content of monosulfide sulfur 99.7%. $(C_5H_{11})_2S$. Calculated %: C 68.96; H 12.64; S 18.39. M 174.

c) Diamyl disulfide 0.49 g (3%).

B.p. 105-106° at 8-9 mm, $d_4^{15}$ 0.9622, $n_D^{15}$ 1.5047.

Found %: C 59.71; H 9.39; S 31.6. M 200; content of disulfide sulfur 95.0%. $(C_5H_{11})_2S_2$. Calculated %: C 58.25; H 10.68; S 31.07. M 206.

d) Diamyl tetrasulfide 2.14 g (18.7%).

B.p. 130-135° at 2 mm, $d_4^{15}$ 1.0342, $n_D^{15}$ 1.5410.

Found %: C 45.52; H 7.64; S 47.17. M 260. $(C_5H_{11})_2S_4$. Calculated %: C 44.44; H 8.15; S 47.40. M 270.

e) Crystalline sulfur 0.82 g (15.6%), m.p. 114°.

f) Residue-sulfur and polysulfides.

Reaction of $H_2S_2$ with cyclohexene. There was used 5.37 g of $H_2S_2$ in 80 ml of cyclohexene. There was isolated: a) $H_2S$ 1.59 g (29.6%).

b) Dicyclohexyl monosulfide 2.36 g (7.75%).

B.p. 97° at 1 mm, $d_4^{15}$ 0.9786, $n_D^{18.5}$ 1.5156.

Found %: C 72.51; H 11.08; S 16.69. M 195; content of monosulfide sulfur 98.9%. $(C_6H_{11})_2S$. Calculated %: C 72.72; H 11.11; S 16.16. M 198.

c) Dicyclohexyl disulfide 1.29 g (7.42%).

B.p. 125-130° at 1 mm, $n_D^{18.5}$ 1.5565.

Found %: C 59.19; H 9.65; S 30.47; content of disulfide sulfur 98.0%. $(C_6H_{11})_2S_2$. Calculated %: C 62.7; S 27.8. H 9.6.

Owing to low volatility, the higher sulfides were not isolated.

## SUMMARY

1. It was shown that the thermal decomposition of hydrogen disulfide in hydrocarbon solvents proceeds through the stage of $\cdot SH$ radicals and $\cdot S_2H$ radicals.

2. It was established that the reactivity of α-olefins in respect to these radicals is much greater than that of β-olefins. The $\cdot SH$ radical does not participate in the reactions of cleavage of hydrogen from hydrocarbons.

3. The products of reaction of hydrogen disulfide with α- and β-pentenes and with cyclohexene were isolated and characterized and the mechanism of their formation was considered.

## LITERATURE CITED

[1] E. B. Milovskaia, B. A. Dolgoplosk and B. L. Erusalimskii, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1957, 494.*

[2] B. L. Erusalimskii, B. A. Dolgoplosk, and A. P. Kavunenko, J. Gen. Chem. 27, 267 (1957).*

[3] G. A. Razuvaev, Iu. A. Ol'dekop and E. I. Fedotova. Progr. Chem. 21, 379 (1952).

[4] E. I. Tiniakova, E. K. Khrennikova, B. A. Dolgoplosk, V. N. Reikh and T. G. Zhuravleva, J. Gen. Chem. 26, 2476 (1956).*

[5] J. Bloch and F. Hohn, Ber. 41, 1965 (1908).

[6] J. Bloch and F. Hohn, Ber. 41, 1975 (1908).

[7] B. A. Kazanskii, A. L. Liberman and A. F. Plate, J. Gen. Chem. 17, 1503 (1947).

[8] Synthesis of Organic Preparations, 1, 335 (1949).**

[9] Organic Syntheses, 1, 183 (1948).**

[10] I. M. Kolthoff and E. B. Sandell, Quantitative Analysis, I, 565 (1948).***

[11] A. A. Vasil'ev, J. Gen. Chem. 17, 923 (1947).

[12] T. Bell and M. S. Agruss, Ind. Eng. Chem. Anal. Ed. 13, 297 (1941).

[13] V. V. Gurova and B. V. Bolotnikov, J. Rubber Ind. No. 6, 61 (1933).

[14] E. B. Milovskaia, B. A. Dolgoplosk and B. L. Erusalimskii, Doklady Akad. Nauk SSSR 120, No. 2 (1958).*

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# ORIENTATION IN AROMATIC RING SUBSTITUTION

## III. ISOMERIZATION OF DICHLOROBENZENES

A. A. Spryskov and Iu. G. Erykalov

When benzene is chlorinated, besides the mono-substituted chloride, a mixture of o- and p-dichlorobenzenes is formed at the ratio of 1 : 2.1 [1]; it also contains a small quantity of meta isomer [2]. In practice it is impossible to change the chlorine orientation successfully and obtain a different ratio of isomers. Orientation may be changed if halogenation is carried out at high temperatures, but the yields are very low. Thus at 450-600° one can get a disubstituted mixture containing 50-60% of meta isomer [3].

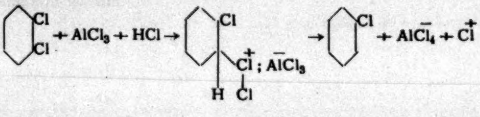
The ratio of isomers can also be changed through isomerization of the disubstituted halides. Thus, for example, when p-dichlorobenzene was heated with lead dioxide at 250-300°, conversion into meta isomer was observed [4]. A similar conversion takes place in the presence of aluminum chloride and hydrogen chloride [5], or in the presence of aluminum chloride alone at 175-250° [6]. The isomerization of o- and p-dichlorobenzenes in the presence of aluminum chloride was patented [7] as a method of preparing m-dichlorobenzene.

In several works the interconversions of 1- and 2-halo derivatives of naphthalene were described [8].

The purpose of the present investigation was to study the isomerization of dichlorobenzenes and to attain an equilibrium state between isomers at different conditions.

Starting with any dichlorobenzene isomer we attained a state of equilibrium between the isomers by heating with aluminum chloride at 160°. The equilibrium mixture contained 16% ortho, 30% para, and 54% of meta isomer. The rate of the isomerization process depended on the quantity of aluminum chloride; when it was increased from 0.1 to 1.5 moles per mole of dichlorobenzene the reaction rate increased, too. During isomerization disproportionation took place; we estimated that experiments in which temperature was kept at 160° during 50 hours yielded about 1.6% of monochlorobenzene. The amount of resin formed can reach 2.8%.

Experimental results provide grounds for the assumption that warming with aluminum chloride produces dehalogenation of dichlorobenzene with the formation of monochlorobenzene and liberation of chlorine. The latter chlorinates monochlorobenzene, forming a mixture of dichlorobenzenes. Dehalogenation proceeds through a donor – acceptor mechanism, as represented by equation



The hydrogen chloride formed in the system resulted from small quantities of moisture absorbed from the air by aluminum chloride. After the reaction tubes were heated, hydrogen chloride was detected.

Thus the chlorination reaction appears reversible in the presence of a catalyst. However, at low temperature the rate of the reverse reaction is so low that for all practical purposes halogenation proceeds irreversibly. With increase in temperature the rate of the reverse reaction (dehalogenation) increases, and isomerization reaction becomes possible; consequently a state of equilibrium can be achieved in the system.

## EXPERIMENTAL

The p-dichlorobenzene used in this work had m.p. 53°. The m-dichlorobenzene (f.p. −25°) was obtained from m-nitroaniline through the Sandmeyer reaction. The o-dichlorobenzene (f.p. −17.8°) was made from o-chloroaniline.

Isomerization experiments were conducted in the following fashion. The three isomeric dichlorobenzenes were introduced separately into three tubes together with aluminum chloride. The sealed tubes were heated in a thermostat, and then their contents was poured out into water acidified with hydrochloric acid (in experiments where considerable resinification occurred, the mixture was filtered with suction). Dichlorobenzene was isolated in a separatory funnel, washed, dried with calcium chloride, and distilled under 12-15 mm pressure into a weighed receiver for the determination of freezing point. If the distilled product would not solidify at room temperature, a fixed quantity of pure para isomer would be added in order to raise the freezing point of the mixture. After freezing-point determination the mixture was nitrated, reduced, and brominated just as previously described [9] for a complete analysis of mixture.

Table 1 lists experimental results from tubes heated at 160°. The experiments showed that in about 50 hours the isomeric system reached a state close to equilibrium.

In experiments where the heating lasted 75 hours, the composition of the mixtures differed very little from that of the previous set. The course of the isomerization process shows that interconversion proceeds fast during the first 15-20 hours, and then slows down considerably.

TABLE 1

Isomerization of Dichlorobenzenes at 160° in the Presence of 0.27 Moles of $AlCl_3$ (20 wt. %).

| Duration of heating hours | Isomer. | Composition of mixture after isomerization (in %) | | |
|---|---|---|---|---|
| | | ortho | para | meta |
| 5 | Ortho | 60.6 | 9.8 | 29.6 |
| | Para | 0 | 74.4 | 25.6 |
| | Meta | 6.0 | 14.2 | 79.8 |
| 15 | Ortho | 28.0 | 24.4 | 47.6 |
| | Para | 3.1 | 60.0 | 36.9 |
| | Meta | 8.4 | 27.3 | 64.3 |
| 20 | Ortho | 24.4 | 25.6 | 50.0 |
| | Para | 4.8 | 47.0 | 48.2 |
| | Meta | 9.8 | 29.3 | 60.9 |
| 30 | Ortho | 20.1 | 27.6 | 52.3 |
| | Para | 10.0 | 33.5 | 56.5 |
| | Meta | 12.9 | 30.4 | 56.7 |
| 50 | Ortho | 16.8 | 29.2 | 54.0 |
| | Para | 14.6 | 30.7 | 54.7 |
| | Meta | 14.9 | 30.6 | 54.7 |
| 75 | Ortho | 18.6 | 28.9 | 52.5 |
| | Para | 17.3 | 29.6 | 53.1 |
| | Meta | 16.9 | 29.5 | 53.6 |

The results of these experiments permit us to establish the following composition of the equilibrium mixture: ortho isomer 16%, para isomer 30%, meta isomer 54%; this composition can be attained by starting from any one of the three isomers. In order to ascertain the stability of such a mixture we made an artificial mixture of 17.5% ortho, 30% para, and 52.5% meta isomers and heated it at 160° during 25 hours. We found the following composition after heating: 19% ortho, 28.9% para, and 52.1% meta isomers, i.e., the composition of mixture was practically unchanged.

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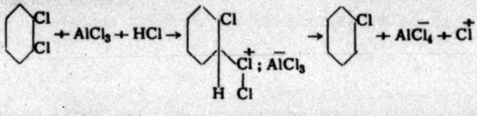

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A second set of isomerization experiments was conducted by heating at 120°. Experimental results (listed in Table 2) show that after heating for 375 hours we were still unable to attain a state close to equilibrium, irrespective of the isomer started with. The isomerization process proceeds much slower at 120° than at 160°.

A third set of experiments was conducted in order to study what effect the amount of catalyst has on the reaction rate. We heated o-dichlorobenzene at 160° during 5 hours with various quantities of aluminum chloride. Experimental results listed in Table 3 show that with increase in the quantity of aluminum chloride the isomerization rate increases rapidly at first, then slowly; finally, 1.5 and 2 moles of aluminum chloride show the same action.

TABLE 2

Isomerization of Dichlorobenzenes at 120° in the Presence of 0.27 moles of $AlCl_3$ (20 wt. %)

| Duration of heating (in hours) | Isomer. | Composition of mixture after isomerization (in %) | | |
|---|---|---|---|---|
| | | ortho | para | meta |
| 25 | Ortho | 77.4 | 4.2 | 18.4 |
| | Para | 2.1 | 96.4 | 1.5 |
| | Meta | 3.2 | 2.9 | 93.9 |
| 50 | Ortho | 71.7 | 6.4 | 21.9 |
| | Para | 0.5 | 93.7 | 5.8 |
| | Meta | 2.2 | 7.7 | 90.1 |
| 100 | Ortho | 55.6 | 11.9 | 32.5 |
| | Para | 0.7 | 90.7 | 8.6 |
| | Meta | 4.1 | 11.1 | 84.8 |
| 200 | Ortho | 33.0 | 17.6 | 49.4 |
| | Para | 1.5 | 81.0 | 17.5 |
| | Meta | 6.0 | 20.3 | 73.7 |
| 375 | Ortho | 25.5 | 22.7 | 51.8 |
| | Para | 5.4 | 45.7 | 48.9 |
| | Meta | 4.1 | 28.5 | 67.4 |

TABLE 3

The Dependence of o-Dichlorobenzene Isomerization Results on the Quantity of $AlCl_3$ used; Reaction Carried 5 hours at 160°

| Moles of $AlCl_3$ taken from each mole of dichlorobenzene | Composition of mixture (in % of isomeric sum) | | | Remainder from the weight of dichlorobenzene taken (in %) |
|---|---|---|---|---|
| | ortho | para | meta | |
| 0.1 | 75.3 | 5.4 | 19.3 | 0.4 |
| 0.25 | 56.1 | 11.9 | 32.0 | 0.5 |
| 0.5 | 37.4 | 21.0 | 41.6 | 0.6 |
| 1.0 | 23.2 | 25.4 | 51.4 | 1.7 |
| 1.5 | 14.0 | 28.2 | 57.8 | 2.3 |
| 2.0 | 14.3 | 28.2 | 57.5 | 2.7 |

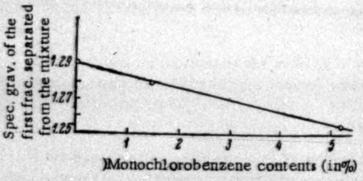
In the same set of experiments we determined the quantity of carbon-like substances formed during isomerization. Having poured the reaction mixture into water, we steam-distilled the dichlorobenzene in an apparatus [10] slightly improved by us. The residue, nonvolatile with steam, was filtered out and weighed. Results of these experiments, listed in the last column of Table 3, show that with increase in the amount of catalyst the quantity of residue increases too, not exceeding, however, 2.7% of the dichlorobenzene used. After heating the meta isomer with 20% aluminum chloride for 200 hours at 120° we found 0.3% of carbon-like substance; the ortho isomer produced 2.8% of this substance when heated 50 hours at 160°.

TABLE 4

Monochlorobenzene Contents, Following Isomerization of o-Dichlorobenzene at 160°

| Moles of $AlCl_3$ taken for each mole of dichlorobenzene | Duration of isomerization (in hours) | Specific gravity of the first fraction | Monochlorobenzene contents (in %) |
|---|---|---|---|
| 0.5 | 5 | 1.2865 | 0.6 |
| 0.5 | 5 | 1.2845 | 0.9 |
| 0.27 | 50 | 1.2794 | 1.6 |

We do not exclude the possibility that during isomerization of dichlorobenzene the disproportionation process goes through the formation of trichloro as well as monochlorobenzenes. Thus in the presence of aluminum bromide, bromobenzene undergoes very extensive disproportionation with the formation of benzene and polybromobenzenes [11]. In our experiments we estimated the degree of disproportionation of dichlorobenzene in the following manner. The vacuum-distilled mixture of dichlorobenzenes was fractionated into two parts. The specific gravity of the first fraction was determined in an Ostwald pycnometer; the amount was 1.4 ml out of 6-6.3 ml distilled off during 1-1.5 hours in a small fractionating column. Artificial mixtures of pure isomeric dichlorobenzenes and chlorobenzene were made up and fractionated. In the artificial mixtures the content of isomers was varied from 37 to 54% for the ortho, 14-21% for the para, and 29-42% for the meta. Large or small contents of individual isomers are hardly reflected at all in the specific gravity. The straight line constructed through three points in the figure represents the specific gravities of the first fractions separated from the artificial mixtures. We estimated the degree of disproportionation by comparing the specific gravity of the experimental first fraction with that of the artificial mixture on the straight line in the figure. The experimental results listed in Table 4 show that the monochlorobenzene content increases if duration of isomerization is increased. The degree of disproportionation was not large and even when the mixture was heated for 50 hours at 160° the monochlorobenzene contents did not exceed 1.6%.



## SUMMARY

Isomerization of o-, m-, and p-dichlorobenzenes in the presence of aluminum chloride at 120 and 160° was studied. During 50 hours at 160° a composition close to that of equilibrium was attained; one could start from any isomer. The equilibrium mixture was composed of 16% ortho, 30% para, and 54% meta isomers. At 120° the isomerization proceeded considerably slower, and the equilibrium mixture was far from being attained.

Isomerization rate was raised when the amount of aluminum chloride increased from 0.1 to 1.5 moles per mole of dichlorobenzene.

During isomerization disproportionation of chlorine was detected. The maximum amount of monochlorobenzene constituted 1.6%. From 0.5 to 2.8% of carbonized residue was formed in the reaction mixture.

## LITERATURE CITED

[1] G. B. Zilberman and G. Ia. Gotlach, Anil. Dye Ind. 5, 285 (1935).

[2] A. F. Holleman and T. Linden, Zbl. 1910, II, 640.

[3] J. P. Wibaut, M. Loon, Nature 139, 151 (1937).

[4] Istrati, Bull. Soc. chim. [3] 3, 186 (1890).

[5] N. N. Vorozhtsov Jr., Chem. Ind. 1947, No. 6, p. 21.

[6] J. Angelkorte, Chim. et ind. 72, 119 (1954).

[7] Am. Pat. No. 2,666,085 (1954); Abstr. J. Chem. 1955, p. 6406.

[8] J. P. Wibaut, F. L. Sixma , and J. F. Suyver, Rec. trav. chim. 68 525 (1949); N. N. Vorozhtsov Jr., et al., J. Gen. Chem. 27, 657, 1787 (1954).

[9] A. A. Spryskov and Iu. G. Erykalov, J. Anal. Chem. 11, 492 (1956).

[10] M. E. Pozzi-Escot, Bull. Soc. Chim. [3] 31, 932 (1904).

[11] F. Fairbrother and N. Scott, Chem.and Ind. 1953,, 998.

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# THE STUDY OF SULFONATION REACTION

## XLVII. THE STUDY OF CHLOROBENZENESULFONIC ACID HYDROLYSIS WITH THE USE OF RADIOACTIVE INDICATORS

A. A. Spryskov and O. I. Kachurin

It is known that the rate of sulfonic acid hydrolysis depends on temperature, the nature and concentration of the mineral acid present, and on the concentration of the sulfonic acid itself [1]. Thus, when the sulfuric acid concentration in the reaction mixture is increased, the hydrolysis rate of sulfonic acid increases too. We showed [2] however, that when the sulfuric acid concentration was increased from 90 to 100% isomerization of m-benzenedisulfonic acid, which proceeds through hydrolysis, was slowed down. During investigation of 1,3,6-naphthalenetrisulfonic acid hydrolysis at 180° it was discovered that by increasing the sulfonic acid concentration to 87.6% one could increase also the quantity of desulfonated acid, but when concentration was further increased to 95.9% the quantity of desulfonated sulfonic acid diminished. However, the latter decrease is connected with the resulfonation of the hydrolyzed product; the rate of sulfonation increases rapidly with increase in the sulfuric acid concentration. The resulfonation interfered with the study of high sulfuric acid concentration effects on the hydrolysis rate of sulfonic acid, since hydrolysis reaction rates were estimated from the quantity of hydrolyzed products or from the increase in the amount of sulfuric acid found in the mixture.

In order to avoid these difficulties, we used sulfuric acid which was labeled with $S^{35}$ isotope. If the chlorobenzenesulfonic acid, mixed with radioactive sulfuric acid, undergoes only hydrolysis when temperature is raised, then the remaining sulfonic acid will remain non-radioactive, and the amount hydrolyzed can be determined from the increase of sulfuric acid. If, however, with increase in sulfuric acid concentration sulfonation reaction begins to take place side by side with hydrolysis, then the chlorobenzenesulfonic acid will become radioactive.

In this manner an increase in the activity of sulfonic acid reflects increased rates of both processes; this can be used to study the effect of concentrated sulfuric acid on the rate of hydrolysis.

## EXPERIMENTAL

In the hydrolysis experiments o-chlorobenzenesulfonic acid was used, because its hydrolysis product (chlorobenzene) is resulfonated with the formation of p-chlorobenzenesulfonic acid only [4], and the para isomer is much harder to hydrolyze than the ortho [5]. The para isomer on repeated hydrolysis changes through resulfonation back into an acid of the same activity. Thus the radioactive indicator method detects only the process in which ortho acid is changed into para.

Experimental mixtures were composed of o-chlorobenzenesulfonic acid and water at a molar ratio of 1:4.5 and varying quantities of anhydrous radioactive sulfuric acid (specific activity 0.15-0.28 in mCu/g) so as to obtain any desired concentration. The mixtures were placed in sealed test tubes and warmed in a thermostat. Samples of reaction mixtures were removed before and after heating, then titrated with 0.1 N alkali to determine the over-all acidity; decrease in acidity would indicate formation of disulfonic acids, while increase was used to calculate the amount of acid hydrolyzed. After heating we dissolved the mixture in water, boiled the solution and treated with excess barium carbonate; the solution was then cooled and the precipitate filtered out and washed. The filtrate and washings were made-up to 50 ml.

To measure the activity we poured the experimental solution on a mica window of a vertically-placed flat counter (type MST-17) in a hollow made of bolted plate-iron walls. A protective cover was placed on top. The thickness of the soultion layer should exceed the maximum range of $S^{35}$ beta particles. Counting time was chosen so that the statistical error would not exceed ± 2% (35-45 minutes). This measuring method was used by us in the 3rd series of experiments.

The 1st series of experiments was conducted by heating the reaction mixture during 10 hours at 150 ± 0.2° and with an experimental accuracy of ± 5%. The experimental results are shown in Fig. 1. Ordinates in Curve 1 were calculated from the total increase in acidity of the mixture. When sulfuric acid concentration is increased the amount of hydrolyzed sulfonic acid increases, attains a maximum in 75% acid, and then diminishes to almost nothing in 87% sulfuric acid. Curve 2, obtained by measuring the activity of sulfonyl chloride isolated from the mixture, shows that in 66% sulfuric acid only hydrolysis takes place since the activity of sulfonic acid is zero. The ordinates of Curve 2 are expressed in terms of the relative specific activity of solution. As the concentration of sulfuric acid in the mixture was raised to 74-76%, the activity of sulfonic acid increased slowly at first and then very rapidly. Thus in about 75% sulfuric acid the resulfonation process starts growing rapidly, becomes observable and measurable. In 89% sulfuric acid the presence of disulfonic acids was detected as well as complete absence of hydrolysis products. At a point corresponding to A in the curve, a break was observed since the activity of disulfonic acid is considerably larger than that of monoacid. From the character of the curve section close to point A one can assume that the resulfonation reaction is slowed down and so is hydrolysis. It is possible that close to point A the hydrolysis reaction rate really decreases and the curve goes through a maximum.

We set up the 2nd series of experiments, in which the mixtures were heated at 126 ± 0.5° during 100 hours, with the purpose of detecting the maximum on the sulfonic acid activity curve and at the same time aiming to avoid disulfonation.

Curve 1 (Fig. 2) shows how the change in the specific molar activity of sulfonic acid depends on the concentration of sulfuric acid in solution; it represents the results of experiments carried out with an accuracy of 2-2.5%. Data from experiments in which disulfonation was absent are joined with the solid line.

Hydrolysis of o-Chlorobenzenesulfonic Acid (with Resulfonation at 119 ± 0.5° During 50 hours in the Presence of Sulfuric Acid and 4.55 Moles of Water per Mole of Sulfonic Acid

| Concentration | | Net counting rate after deduction of control (in counts/minute) | Specific molar activity (in counts/liter min·mmole). |
|---|---|---|---|
| of sulfuric acid (in %) | of meas. solution (in mmoles/liter) | | |
| 85.4* | — | 6.4 ± 1.6 | — |
| 85.4 | 44.1 | 511 ± 8 | 11.6 ± 0.2 |
| 86.2 | 37.7 | 612 ± 10 | 16.2 ± 0.3 |
| 87.1 | 26.6 | 569 ± 17 | 21.4 ± 0.6 |
| 87.5 | 23.0 | 494 ± 8 | 21.5 ± 0.3 |
| 88.5 | 20.5 | 497 ± 8 | 24.2 ± 0.4 |

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*Control: the reaction mixture was not heated, but measured as described.

The last data were determined in 88% acid and therefore the results of this experiment are joined to the remaining ones by a dotted line. Thus the curve shows a maximum in degree of resulfonation which reflects the hydrolysis reaction rate.

The attempt to obtain a more precise maximum induced us to set up a 3rd series of experiments in which the mixture was heated during 50 hours at 119 ± 0.5°.

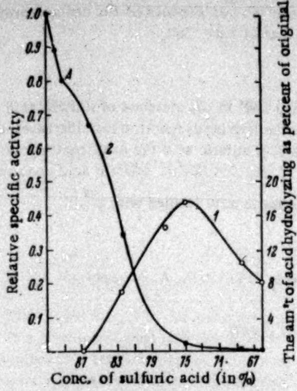

Fig. 1. Change in the relative hydrolysis reaction rate of o-chlorobenzenesulfonic acid in the presence of sulfuric acid at 150°. 1) The amount of hydrolyzed sulfonic acid found from the over-all increase in acidity of mixture; 2) relative specific activity of chloride separated from the mixture.

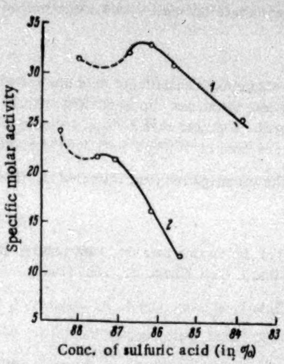

Fig. 2. Change in the relative hydrolysis reaction rate of o-acid at 119 and 126°. 1) Change in specific molar activity of sulfonic acid in reaction mixture after 100 hours at 126°; 2) change in specific molar activity of sulfonic acid in reaction mixture after 50 hours at 119°.

The experimental results, listed in the table and shown as Curve 2 in Fig. 2, indicate that in 87.5% sulfuric acid no increase in sulfonic acid activity takes place as compared to the preceding run in 87.1% acid.

On Curve 2 (Fig. 2) a sharp change in the curve direction occurs, but we were still unable to obtain a precise maximum since in the subsequent run (in 88.5% sulfuric acid) the presence of disulfonic acids became noticeable again.

The correction for isotope dilution was computed in experiments of 2nd and 3rd series but turned out very small and therefore was not included in the results. Approximate calculations give the degree of resulfonation, i.e. for the hydrolyzed and resulfonated part of the whole acid, in the range of 42-54% for the 2nd set of experiments, and 16-54% for the 3rd.

## DISCUSSION OF RESULTS

On the basis of our experimental results we can assume that the rate of the sulfonic acid hydrolysis increases with the increase in sulfuric acid concentration, attains a maximum and then decreases. The hydrolysis rate maximum for o-chlorobenzenesulfonic acid was observed at a sulfuric acid concentration of approximately 87% in the 120-150° temperature range.

Earlier [2] we have recorded an increase in the isomerization rate of m-benzenedisulfonic acid when the concentration of sulfuric acid was decreased from 100 to 90%. The equilibrium constant for the reaction $H_2SO_4 + H_2O \rightleftarrows H_3O^+ + HSO_4^-$ in concentrated sulfuric acid solutions was calculated:

$$K = \frac{[H_3O^+][HSO_4^-]}{[H_2O]} = 1.2 \text{ mole/kg.}$$

With the usual assumptions we calculated the $H_3O^+$ concentration in sulfuric acid containing from 5 to 30% water by introducing the molar concentration (10.2) of sulfuric acid into the equation; we found out that when the sulfuric acid is diluted the $H_3O^+$ concentration has a maximum in 80% sulfuric acid. Taking into consideration the assumptions made, the various temperatures of hydrolysis and of experiments run to calculate the equilibrium in sulfuric acid, and also the presence of sulfonic acid in sulfuric, we can presume that there exists in sulfuric acid a well known correspondence between the type of $H_3O^+$ concentration curve and the rate of sulfonic acid hydrolysis [5], according to which the hydrolysis reaction rate depends on the concentration of the intermediate complex whose concentration in turn depends on that of $H_3O^+$ ion.

## SUMMARY

o-Chlorobenzenesulfonic acid was hydrolyzed at 119, 126, and 150° in the presence of sulfuric acid of varying concentrations. Up to 86-87% sulfuric acid concentrations the hydrolysis reaction rate increases, then the increase stops and even a slight decrease begins. Starting with 88% sulfuric acid the disulfonation reaction prevents us from obtaining a well defined maximum on the curve of reaction rate vs. sulfuric acid concentration.

The investigation was conducted radiometrically; we used sulfuric acid labeled with $S^{35}$.

## LITERATURE CITED

[1] J. M. Crafts, Ber. 34, 1350 (1901); Bull. Soc. Chim. [4] 1, 917 (1907); A. A. Spryskov and N. A. Ovsiankina, J. Gen. Chem. 21, 1508 (1951).

[2] S. P. Starkov and A. A. Spryskov, J. Gen. Chem. 27, 3067 (1957).

[3] R. Lantz, Bull. Soc. chim., [5] 14, 98 (1947).

[4] A. F. Holleman, Chem. Revs. 1, 187 (1924).

[5] A. A. Spryskov and N. A. Ovsiankina, J. Gen. Chem. Supp. II, 882 (1953).

[6] R. J. Gillespy, J. Chem. Soc. 1950, 2493.

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# MECHANISM OF α-TETRALOXIME CONVERSION INTO α-NAPHTHYLAMINE

N. N. Vorozhtsov and V. A. Koptiug

The conversion of cyclic ketoximes possessing one double bond in a six-membered ring or a heterocyclic sulfur in a five-membered ring into aromatic amines has been known for a fairly long time and has been suitably applied to a large number of compounds. The conditions described in the literature for effecting this conversion are extremely diverse. Thus carvenoxime hydrochloride changes into carvacrylamine hydrochloride on dry distillation [1]; 1,2,3,4-tetrahydroquinoloxime-4 gives 4 aminoquinoline when warmed with activated charcoal in vacuo [2]; isophoroxime changes into 3,4,5-trimethylaniline when heated to 170° with 20% hydrochloric acid [3] (however, compare [4]); thujoxime gives carvacrylamine when heated in 50% alcoholic sulfuric acid solution [5]; 1-phenyltetraloxime-2 changes into 1-phenylnaphthylamine-2 hydrochloride when heated with hydrogen chloride in absolute alcohol [6]. With a number of 3-ketotetrahydrothiophene derivatives the conversion into the corresponding 3-aminothiophenes takes place when hydrogen chloride is introduced into an ether solution of the oxime [7]. Oximes of substituted cyclohexenones change into corresponding N-acetanilides when warmed with acetyl chloride [3], acetic anhydride [3, 8], acetic anhydride and sodium acetate [9], and also on interaction with acetyl chloride in acetic anhydride in the presence of pyridine [4] (compare [10]). Schroeter and co-workers [11] showed that oximes of α-tetralone and of its derivatives (except 8-substituted) change into corresponding α-naphthylamines on treatment with "Beckmann's mixture" (solution of acetic anhydride in glacial acetic acid saturated with hydrogen chloride) at 100° (see also [7, 12]). The sulfate of α-tetraloxime changes into α-naphthylamine under the action of hydrogen chloride in dioxane [13].

The mechanism by which ketoximes are converted into aromatic amines has not been elucidated until now.

We investigated the conversion of α-tetraloxime into α-naphthylamine under conditions described by Shroeter and co-workers [11], i.e., by heating it at 100° with 1.3 moles of acetic anhydride in glacial acetic acid in the presence of hydrogen chloride. The reaction mass obtained in this manner yielded 2-chloro-1-keto-1,2,3,4-tetrahydronaphthalene (I, approx. 2.0%) and 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole (II, 8.6%) besides previously [11] detected α-naphthylamine hydrochloride (31.0%) and N-acetyl-α-naphthylamine (3.3%). (I) was identified in the form of oxime which was prepared by the method described for 2-bromo-1-keto-1,2,3,4,-tetrahydronaphthalene [14].

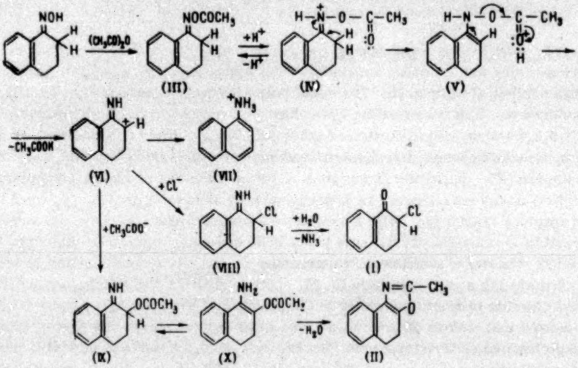
The structure of the previously undescribed compound (II) was determined by dehydrogenation with diphenyldisulfide (see [15]) into 2-methyl-(naphtho-1',2':4,5-oxazole) (yield 87.5%, identified as picrate and methiodide), and through synthesis (yield 12.7%) from 2-bromo-1-keto-1,2,3,4-tetrahydronaphthalene (see [16] for method of obtaining oxazoles).

Since one of the methods used to obtain oxazoles consists of heating α-haloketones with ammonium formate in formic acid [17, then one could presume that during conversion of α-tetraloxime into α-naphthylamine, compound (II) results from the interaction between compound (I), acetic acid, and ammonium chloride; ammonium chloride was detected among reaction products (16.4% yield, based on α-tetraloxime). We heated (I) with ammonium chloride (and also with acetamide) in acetic acid in a stream of hydrogen chloride but were unable to obtain (II).

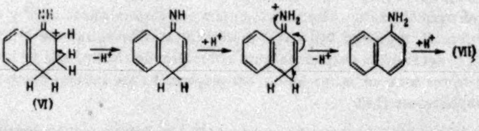
Compound (II) in its turn, could not be an intermediate product in the formation of α-naphthylamine since it does not undergo any change when heated in acetic acid with hydrogen chloride.

Determination of the nature of side products will permit a better understanding of the mechanism by which α-tetraloxime is converted into α-naphthylamine. The first reaction product is O-acetyl derivative of α-tetraloxime (III),* which precipitates in the form of white crystals when acetic anhydride is added to the solution of oxime in glacial acetic acid. Since acetic anhydride is not required in further conversion of O-acetyl derivative (III) into α-naphthylamine (see experimental part), then it follows that the function of acetic anhydride consists of oxime acetylation.

The O-acetyl derivative of α-tetraloxime does not change when heated at 100° in glacial acetic acid. But under the same conditions it will change to α-naphthylamine (and side products) if hydrogen chloride is present. The mechanism of this conversion can be described by the following scheme:



The attack of a proton on the nitrogen in the acetyl derivative of the oxime (III) and the subsequent electron displacement result in a transfer of hydrogen (in the form of a proton) from a ring carbon to the oxygen in the acetyl group, as shown by structures (IV) and (V); after this, acetic acid is split-out and a carbonium ion is formed (VI). As a result of proton transfer, the last one isomerizes into naphthylammonium ion (VII),



while with $Cl^-$ and $CH_3COO^-$ anions it changes into 2-chloro- and 2-acetoxy-1-imino-1,2,3,4-tetrahydronaphthalene, respectively (VIII and IX). The tautomeric form of (I) – 1-amino-2-acetoxy-3,4-dihydronaphthalene (X), changes into (II) by splitting out a molecule of water. Formation of the last one should proceed fairly easily, since it is known that the aromatic analog of (X) – 1-amino-2-acetoxynaphthalene – cannot be obtained since it readily converts into the corresponding oxazole [18]. In water (VIII) hydrolyzes to (I).

It is hardly possible under these conditions to split out hydrogen chloride from (VIII) and form α-naphthylamine, for the 2-halo-1-keto-1,2,3,4-tetrahydronaphthalenes are characterized by a comparatively small tendency to dehydrohalogenate [19].

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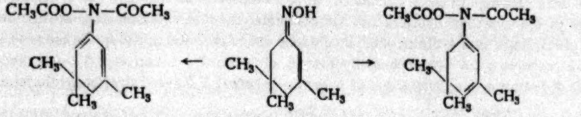
*Schroeter and co-workers [11] assumed that the reaction starts with addition of hydrogen chloride to the oxime or to its acetyl derivative.

The proton donor in the examined reaction is hydrogen chloride; this is obvious from comparison of following data. The dissociation constant of 100% acetic acid is ~$1.43 \times 10^{-14}$ at 25°*, while that of hydrogen chloride in 100% acetic acid equals $5.1 \times 10^{-10}$ [21], i.e. $3.5 \times 10^4$ times larger. This explains why in the absence of hydrogen chloride the acetyl derivative of the oxime does not change into α-naphthylamine.

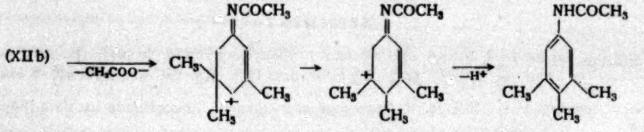
It has been noted [11] that the p-toluenesulfonyl derivative of α-tetraloxime undergoes normal Beckmann rearrangement under the same conditions that lead to the conversion of oxime acetate into α-naphthylamine. From the point of view of the proposed mechanism, this can be explained by a decrease in the basicity of the oxime nitrogen (low to begin with) when the acetyl group is replaced with a more electrophilic p-toluenesulfonyl radical; as a result, the ability of a proton to attack the oxime nitrogen is reduced.

One should note that in the opinion of investigators [4] the conversion of isophoroxime (XI) into a mixture of N-acetyl derivatives of 2,3,5- and 3,4,5-trimethylaniline under the action of acetyl chloride and pyridine in acetic anhydride evidently proceeds also through the formation of a carbonium ion intermediate. These authors put forward a working hypothesis that the reaction begins with the formation of hypothetical O,N-diacetyl derivatives of isophoroxime (XII a,b)



(XIIa) (XI) (XIIb)

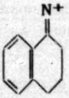
and proceeds as below,



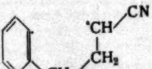
Compound (XII a) changes into N-acetyl-2,3,5-trimethylaniline in a similar fashion.

Migration of the methyl group, observed in this case, is a strong argument in favor of a carbonium ion intermediate. But the formation of O,N-diacetyl derivatives of the oxime seems questionable to us. It is natural to assume that the conversion in this case proceeds through a monoacetyl oxime derivative with the formation of amine, which then undergoes acetylation.

Hardy and co-workers [12] have recently repeated the conversion of 7-nitrotetraloxime-1- into 7-nitronaphthylamine-1 (described by Schroeter [11]) and came out with the hypothesis that aromatization proceeds through the formation of an intermediate ion (XIII) or a biradical (XIV).



(XIII)



(XIV)

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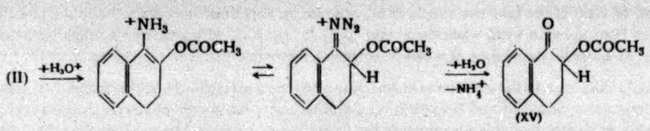
*Calculated from the autoprotolysis constant $[CH_3COOH_2^+] \cdot [CH_3COO^-] = 2.5 \cdot 10^{-13}$ [20].

However, neither hypothesis makes it possible to explain the formation of the reaction products we isolated (not to mention other serious shortcomings in the scheme of Hardy and co-workers).

We obtained some interesting results while studying the reactions of 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole (II). We found out that when it was boiled with hydrochloric acid, β-naphthol formed readily (91% yield). This unexpected conversion was explained as follows: acidic cleavage of (II) forms 2-acetoxy-1-keto-1,2,3,4-tetrahydronaphthalene (XV) as a first step.



The conversion of the latter into β-naphthol, caused by boiling it with hydrochloric acid, has already been described [22].

If the acid cleavage of (II) is carried out at room temperature with the use of dilute hydrochloric acid in the presence of 2,4-dinitrophenylhydrazine hydrochloride, then the reaction stops at the ketone (XV) stage; the ketone precipitates as 2,4-dinitrophenylhydrazone out of reaction mixture. In order to identify the product obtained, we prepared a 2,4-dinitrophenylhydrazone of 2-acetoxy-1-keto-1,2,3,4-tetrahydronaphthalene by starting with 2,4-dinitrophenylhydrazone of 2-bromo-1-keto-1,2,3,4-tetrahydronaphthalene [23].

The cleavage of the N–C bond in oxazole (II) is somewhat unexpected since acids usually cleave the O–C in oxazoles. In particular, one should have expected (see [16]) to form the 2,4-dinitrophenylhydrazone of 1-acetamide-2-keto-1,2,3,4-tetrahydronaphthalene by the action of dilute hydrochloric acid on oxazole (II) in the presence of 2,4-dinitrophenylhydrazine.

## EXPERIMENTAL

α-Tetralone was obtained through cyclization of γ-phenylbutyrylchloride [24]; the yield was 92.5% b.p. 110.5-112.5° at 5 mm, $n_D^{20}$ 1.5691. According to lit. data [25]; b.p. 105° at 3 mm, $n_D^{20}$ 1.5691, 1.5693.

Oxime: yield 94%, m.p. 100.5-101.5° (from aqueous methanol). According to lit. data [25]: m.p. 102.5-103.5°.

Elucidation of the acetic anhydride and hydrochloric acid role in the conversion of α-tetraloxime into α-naphthylamine. Experiment 1. We added 2.25 ml of acetic anhydride to a solution containing 3.0 g of α-tetraloxime in 19.0 ml of 99.8% acetic acid at room temperature. In about 1-1.5 minutes a white O-acetyl derivative of the oxime (III) precipitated. The yield was 3.7 g (97.5%), m.p. 144.0-144.5°. According to lit. data [11]: m.p. 148°. Experiment 2. We dissolved 1.5 g of the oxime acetyl derivative in 7.5 ml of hot 99.8% acetic acid and kept the solution for 10 min in a 110° bath; at the same time hydrogen chloride was bubbled through it. When the solution cooled, slightly greyish crystalline α-naphthylamine precipitated (see below for identification); the yield was 0.48 g (36.2%). Experiment 3. After mixing 2.5 g of α-tetraloxime acetyl derivative, 0.34 ml of acetic anhydride, and 12.5 ml of 99.8% acetic acid we heated them for 1 hour in a 110° bath. We isolated 1.80 g (72%) of the starting material, m.p. 144-145°, from the reaction mixture diluted with water.

Investigation of the α-tetraloxime conversion products. Experiment 4. The reaction was carried out in a four-necked flask provided with a reflux condenser, a thermometer, a stirrer, and a tube to introduce hydrogen chloride under the liquid surface.

To a 50 g solution of α-tetraloxime in 310 ml of 99.6% acetic acid 37.5 ml of acetic anhydride was added. After 1-1.5 minutes the whole mixture solidified due to the formation of the acetyl derivative of oxime (III). When after 45 minutes the bath temperature was raised to 100° the acetyl derivative went into solution which gradually acquired a violet-red color. Having turned the stream of hydrogen chloride on (50-70 ml/min.), we maintained the reaction mixture at 100° for 2 hours. During this time the reaction mixture gradually darkened, and eventually became almost black. The grey crystalline precipitate of α-naphthylamine hydrochloride, which formed when the solution was cooled, was filtered out and washed with 100 ml of glacial acetic acid. The weight of precipitate was 14.90 g. When we benzoylated 0.50 g of it in the usual manner, we obtained 0.67 g (97.5%) of the benzoyl derivative of α-naphthylamine, m.p. 159-160° after recrystallization from ethyl alcohol. According to lit. data [26]: m.p. 161°.

After removing α-naphthylamine hydrochloride we distilled off in vacuo (bath temperature 80°) the acetic acid from the filtrate. We triturated the resinous residue (a ) with 50 ml of chloroform; the precipitate that formed was filtered out and washed with 25 ml of chloroform. The grey crystalline precipitate weighed 4.0 g. From 0.50 g of the precipitate we obtained on benzoylation 0.21 g (30.5%) of N-benzoyl-α-naphthylamine, m.p. 151-153°. Besides this, the precipitate contained ammonium chloride (68% by weight of precipitate) and did not contain any hydroxylamine hydrochloride (qualitative test with iodine and sulfanilic acid). The ammonium chloride content was determined in the usual fashion by distilling off the amine from an alkaline solution (diazotization was used to determine the amount of co-distilled α-naphthylamine). The ammonium chloride yield was 2.72 g of 16.4% if computed from α-tetraloxime.

The chloroform filtrate was extracted with 0.5 N hydrochloric acid solution (10 portions of 30 ml each). The hydrochloric solution was washed with chloroform and ether, treated with solid sodium carbonate until it became alkaline, and extracted with ether. When hydrogen chloride (dried over anhydrous sodium sulfate) was passed through the ether solution a crystalline precipitate of α-naphthylamine hydrochloride formed; the weight was 1.1 g. Benzoylating 0.22 g of it, we obtained 0.27 g (89%) of N-benzoyl-α-naphthylamine, m.p. 159.5-160.5°; after recrystallization from ethyl alcohol. Thus the over-all yield of α-naphthylamine was ~17.2 g (31.0%).

After extraction with hydrochloric acid the chloroform solution was washed with 10% sodium carbonate solution and then with water. The chloroform was distilled off in vacuum (bath temperature 50°) and the residue steam-distilled. A black tarry residue (b) remained in the flask. The oil that distilled off with 2 liters of distillate was extracted with ether. When hydrogen chloride (dried over anhydrous sodium sulfate) was passed into the ether solution of slightly greyish precipitate (v) formed; it weighed 9.90 g. The precipitate obtained contained ~60% of 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole hydrochloride ( ~8.6% yield) and practically no α-naphthylamine hydrochloride.

The oxazole hydrochloride contents in the precipitate was determined from the picrate yield (0.66 g of picrate, m.p. 143.5-144.5, were obtained from 0.56 g of precipitate) and also from the yield of β-naphthol formed when precipitate (v) was boiled with dilute hydrochloric acid (1 : 1) (from 1.02 g of precipitate (v) 0.34 g of β-naphthol was obtained). We were not able to separate the pure oxazole by fractionating the base obtained from precipitate (v). (Isolation of oxazole in a pure form is described in experiment 5).

Having removed precipitate (v) we washed the ether filtrate with 5% sodium bicarbonate solution and water, dried with sodium sulfate, and concentrated by evaporation. Fractional distillation of the residue (in a Claisen flask with a 7 cm fractionating column) gave the following fractions: 1st b.p. 125-132° at 14 mm; weight 4.64 g; 2nd. b.p. 132-152° at 14 mm, weight 1.13 g; 3rd b.p. 152-162° at 14 mm, weight 2.22 g; residue 1.5 g of a brown viscous oil.

1st Fraction – colorless mobile liquid which, as the boiling point would indicate, must be α-tetralone The literature [25] gives b.p. 134° (at 15 mm) for α-tetralone. When we boiled (30 minutes ) 1.45 g of the 1st fraction with 1.4 g of hydroxylamine hydrochloride and 1.5 g of potassium carbonate in a mixture of 9 ml methanol and 6 ml water, we obtained 1.43 g (89.3%) of α-tetraloxime which had a m.p. 101-102° after recrystallization from dilute methanol. This sample if mixed with known α-tetraloxime produced no melting point depression. The yield of α-tetralone was 10.2%.

3rd Fraction – colorless viscous oil containing halogen (Beilstein's test). The oil was soluble in ether and in methanol but not in petroleum ether. Skin irritating action as well as boiling point would permit us to assume that the 3rd fraction contains 2-chloro-1-keto-1,2,3,4-tetrahydronaphthalene (I). The literature reports [27] b.p. 157-160° (at 14 mm) for this ketone. To a 1.25 g solution of the 3rd fraction in 15 ml of methanol we added 1.25 g of hydroxylamine hydrochloride dissolved in 2 ml of water; the clear solution was left standing 24 hours at room temperature. After this we diluted it with 20 ml of water and extracted the oil that separated-out, three times with 3 ml portions of chloroform. When hydrogen chloride was bubbled through the chloroform solution a white crystalline precipitate of oxime hydrochloride formed; the yield was 0.78 g m.p. 124-130° (in a sealed capillary). To convert the hydrochloride into free oxime we dissolved it in 6 ml of methanol and diluted with 6 ml of water. A white crystalline precipitate formed; its yield was 0.36 g m.p. 105-118°. Recrystallization from petroleum ether (b.p. 80-100°) gave white needles, m.p. 117.5-118.5°.

Found %: N 7.20, 7.34. $C_{10}H_{10}ONCl$. Calculated %: N 7.16.

A sample of it mixed with known oxime of 2-chloro-1-keto-1,2,3,4-tetrahydronaphthalene (see below) did not lower the melting point.

Thus the third fraction contained 2-chloro-1-keto-1,2,3,4-tetrahydronaphthalene (~50% by weight); its yield was 2.0%. We extracted 1.90 g (3.3%) of N-acetyl-α-naphthylamine from the tarry residue (b) using boiling water (10 times with 50 ml samples). The N-acetyl-α-naphthylamine m.p. 158-159° (recrystallized from methanol). According to literature [26]; m.p. 160°.

A sample mixed with known N-acetyl-α-naphthylamine did not lower the melting point.

After the remainder of residue (b) was made alkaline, a black brittle resin remained which was soluble in chloroform but not in hot methanol or glacial acetic acid – the yield, 11.2 g.

Experiment 5. It was similar to experiment 4. The residue (a) was treated with 100 ml of ether and 200 ml of water. After shaking for 15 minutes we filtered it, separated the ether layer, and extracted the aqueous layer with ether (twice with 50 ml samples). The ether extracts were dried over anhydrous sodium sulfate, and then hydrogen chloride was bubbled through producing a precipitate (g) of 2-methyl-3',4'-dihydronaphtho-1', 2',:4,5-oxazole; its yield was 8.9 g (13%). When placed in water the hydrochloride hydrolyzed producing an oily base. The hydrochloride was triturated with water, the precipitate produced extracted with ether, and vacuum-distilled in a flask outfitted with a Claisen head and an 8 cm fractionating column. We obtained a colorless liquid posessing a peculiarly pleasant odor; its yield was 5.5 g (9.6%).

Analysis and molar refractions correspond to those calculated for 2-methyl-3',4'-dihydronaphtho-1',2': 4,5-oxazole (II):

B.p. 104° at 0.5 mm, $d_4^{18}$ 1.1855, $n_D^{18}$ 1.5948, $MR_D$ 53.07; calculated 53.47.

Found %: C 77.40, 77.30; H 5.97, 6.12; N 7.57, 7.69. $C_{12}H_{11}ON$. Calculated %: C 77.80; H 5.99; N 7.56.

The picrate of oxazole (II) was made from 0.245 g of oxazole and 0.303 g of picric acid in 6 ml of absolute ethyl alcohol; the yield was 0.485 g (88.5%). Recrystallized from absolute ethyl alcohol it gave yellow needles, m.p. 145.5-146.0°.

Found %: C 52.05, 52.20; H 3.57, 3.68; N 13.35, 13.43. $C_{18}H_{14}O_8N_4$. Calculated %: C 52.18; H 3.41; N 13.52.

Methyl iodide derivative of oxazole (II). We heated 0.13 g. of methyl iodide with 0.29 g of oxazole (II) in a sealed glass ampule for 18 hours in a 115-125° bath. The precipitate obtained was transferred to a filter paper and washed with ether and acetone. We obtained small colorless needles, m.p. 210.0-211.5° (it remained the same after recrystallization from absolute ethyl alcohol); the yield was 0.43 g (84%).

Found %: C 47.91, 48.02; H 4.40, 4.51. $C_{13}H_{14}ONI$. Calculated %: C 47.72; H 4.31.

A sample of this derivative when mixed with some 2-methyl-(naphtho-1',2':4,5-oxazole) methiodide (m.p. 210.1-211.5°, see below) melted at 202-203°.

Hydrochloride of oxazole (II) was made by bubbling hydrogen chloride through an ether solution of the b base; its m.p. 222-224° (in a sealed capillary, introduced at 180°). A substance with the same melting point was obtained when hydrochloride (g) was recrystallized from acetone (thin needles).

Found %: ionizable Cl 15.9, 160. $C_{12}H_{12}ONCl$. Calculated %: Cl 15.99.

The hydrochloride was soluble in chloroform and glacial acetic acid, but not in benzene and ether.

Dehydrogenation of 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole (II) into 2-methyl-(naphtho-1', 2':4,5-oxazole). We heated 0.30 g of 2-3',4'-dihydronaphtho-1',2':4,5-oxazole with 0.53 g of diphenyldisulfide for 2 hours in a sealed glass tube at 260-265°. The reaction mixture was a yellow liquid with a strong odor of thiophenol; it was dissolved in 8 ml of ether through which hydrogen chloride was allowed to bubble. The precipitate that formed was filtered out and washed with ether until the odor of thiophenol disappeared. We obtained 0.31 g (87.3%) of 2-methyl(naphtho-1',2':4,5-oxazole) hydrochloride (XIV), m. p. 164-174° (in a sealed capillary). According to lit. data [28]: m.p. 177°.

We converted 0.13 g of the hydrochloride (XIV) into the free base: treatment of the base with 0.14 g of picric acid in 4 ml of absolute ethyl alcohol produced the picrate of 2-methyl-(naphtho-1',2':4,5-oxazole), the yield of which was 0.204 g (83.8%). Recrystallization from absolute ethyl alcohol gave yellow needles, m.p. 148.5-149.5°. A sample of it mixed with 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole picrate melted at 135-137°. A sample mixed with known 2-methyl- naphtho- 1',2':4,5-oxazole) picrate (see below) did not lower the melting point.

Found %: N 13.76, 13.86; $C_{18}H_{12}O_8N_4$. Calculated %: N 13.59.

The free base obtained from 58 mg of hydrochloride (XIV) and 0.1 ml of methyl iodide were heated in a sealed glass tube during 15.5 hours in a bath at 115-125°. This yielded 40 mg (46.5%) of 2-methyl-(naphtho-1'2':4,5-oxazole) methiodide. The m.p. was 205-206° after recrystallization from absolute ethyl alcohol (purification is difficult due to the instability of the product [29]). A sample mixed with known 2-methyl-(naphtho-1',2':4,5-oxazole) methiodide (see below) did not lower the melting point.

A mixture containing 75 mg of hydrochloride (XIV), 1.5 ml of ethyl alcohol, and 0.5 ml of 12% hydrochloric acid was boiled with refluxing for 10 minutes. The resulting solution was evaporated down to 1 ml and diluted with 5 ml of water. A white precipitate was filtered out, washed with 12% hydrochloric acid solution, and dried out; the yield was 35 mg. After recrystallization from dilute methyl alcohol the m.p. was 228.5-230.0°. A sample of it when mixed with some 1-acetaminonaphthol-2 (m.p. 235-236°) produced no melting pount depression. According to lit. data [28]: m.p. 235°.

The action of acids on 2-methyl-3',4'-dihydronaphto-1',2':4,5-oxazole (II). A solution of 208.4 mg of oxazole (II) in 5 ml of hot concentrated hydrochloric acid was boiled for 2 hours with refluxing. When the solution was cooled a pink precipitate formed which was extracted with ether. Evaporation of ether yielded 148.0 mg (91.0%) of β-naphthol, m.p. 110-111°. The β-naphthol that formed did not produce coloration with p-toluenediazonium chloride in acetic acid [30]; this would indicate the absence of any α-naphthol in the sample. After reprecipitation from an alkaline solution and one recrystallization from water, the m.p. 120.0-121.0°. When mixed with a known sample of β-naphthol it did not lower the melting point. Having removed the β-naphthol we determined the amount of ammonia present in the hydrochloric acid solution; the quantity was 91.5% of theoretical.

Boiling of oxazole (II) with dilute hydrochloric acid (1:1) leads to the same results.

Oxazole (II) does not undergo any change when heated in glacial acetic acid saturated with hydrogen chloride. After heating it for 4 hours at 110-115° we recovered 87.5% of the starting material. No β-naphthol was detected.

Interaction of 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole (II) with hydrochloric acid and 2,4-dinitrophenylhydrazine. A solution containing 0.72 g of 2,4-dinitrophenylhydrazine in 144 ml of 2 N hydrochloric acid was added to 0.72 g of oxazole (II) hydrochloride dissolved in 14.4 ml of 2 N hydrochloric acid and 50 ml of water. After 2 months an orange precipitate formed; yield 0.26 g, m.p. 140-150°. Two recrystallizations from ethyl acetate gave red crystals, m.p. 185-186°. A sample mixed with 2,4-dinitrophenylhydrazone of 2-acetoxy-1-keto-1,2,3,4-tetrahydronaphthalene (see below) did not depress the melting point.

Found %: N 14.64, 14.82. $C_{18}H_{16}O_6N_4$. Calculated %: N 14.58.

The action of potassium hydroxide on oxazole (II). We boiled 134.5 mg of oxazole for 3 hrs. in a 5 ml of 30% potassium hydroxide solution. We recovered 84% of the starting material from the reaction mixture; it was isolated as hydrochloride, m.p. 222-224° We were unable to detect any β-naphthol.

Examination of the possibility to form oxazole (II) from (I) under the reaction conditions. A mixture containing 1.0 g of (I), 0.296 g of ammonium chloride, and 6 ml of 99.5% acetic acid was kept in a 100° bath for 2 hours with hydrogen chloride bubbling through it (18 ml/min). The acetic acid was distilled off in vacuo, the residue treated with 10% sodium carbonate, and extracted with ether. No precipitate formed when hydrogen chloride was passed through the ether solution which had been dried over anhydrous sodium sulfate.

Nor was any oxazole (II) detected among reaction products when equimolar quantities of (I) and acetamide in acetic acid were treated in the above described fashion.

The preparation of 2-chloro-1-keto-1,2,3,4-tetrahydronaphthalene (I) and its oxime. We obtained (I) by chlorinating α-tetralone [32]. The unpurified product melted at 38-41°; according to lit. data [32] for the pure product: m.p. 44-45.5°.

We dissolved 0.60 g of the prepared product and 0.60 g of hydroxylamine hydrochloride in a 9 ml methanol - 0.7 ml water mixture and left the resulting clear solution at room temperature for 24 hours. White oxime precipitated when the solution was cooled to 0° and diluted with 25 ml of cold water; the yield was 0.59 g (91.0%), m.p. 104-111°. After two-fold recrystallization from petroleum ether (60-80° fraction) we obtained tiny white needles, m.p. 120.0-120.5°.

The preparation of 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole (II). Using a condenser outfitted with a calcium chloride tube we refluxed 2 g of 2-bromo-1-keto-1,2,3,4-tetrahydronaphthalene (obtained through bromination of α-tetralone [33]; yield 82.5%, m.p. 37-39°)with 1.2 g of acetamide in a 140° bath for 3 hours. The reaction mixture was shaken up with 10 ml of 10% sodium carbonate and 5 ml of benzene. The benzene layer was separated, washed with water, and dried over anhydrous sodium sulfate. When hydrogen chloride was bubbled through the benzene solution, 0.25 g (12.7%) of 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole hydrochloride was formed.

The hydrochloride was converted into free base and made into picrate; after recrystallization from absolute ethyl alcohol the m.p. 144.5-145°. When a sample of it was mixed with some picrate of 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole obtained from conversion of α-tetraloxime, no melting point depression was observed.

2-Methyl-(naphtho-1',2':4,5-oxazole) was prepared from 1-aminonaphthol-2 hydrochloride [29]; the yield was 50%, b.p. 161° at 15 mm; according to lit. data [28]: b.p. 158° at 14 mm.

Methiodide, the yield was 41.3%, m.p. 210.5-211.5°; according to lit data [29]: m.p. 212-213°;

Picrate, the yield was 94.5%, m.p. 148.3-149.5°.

2,4-Dinitrophenylhydrazone of 2-acetoxy-1-keto-1,2,3,4-tetrahydronaphthalene was made by starting with 2,4-dinitrophenylhydrazone of 2-bromo-1-keto-1,2,3,4-tetrahydronaphthalene (see [19]; 70% yield, m.p. 180.5-181.5°) and boiling it with anhydrous ethyl acetate (10% excess) for 20 minutes in glacial acetic acid. The yield was 90.8%. Recrystallization from ethyl acetate gave orange-red prisms, m.p. 185-186°; according to lit. data [23]: m.p. 186-187°.

## SUMMARY

1. When α-tetraloxime was heated with acetic anhydride in glacial acetic acid, in the presence of hydrogen chloride, the following were formed: α-naphthylamine, N-acetyl-α-naphthylamine, α-tetralone, 2-chloro-1-keto-1,2,3,4-tetrahydronaphthalene, and 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole.

2. The structure of 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole was determined by dehydrogenation with diphenyldisulfide into 2-methyl-(naphtho-1',2':4,5-oxazole) and by synthesis from 2-bromo-1-keto-1,2,3,4-tetrahydronaphthalene and acetamide.

When boiled with hydrochloric acid, 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole was converted into β-naphthol.

3. A mechanism which explains the formation of all the isolated products is proposed for the conversion of α-tetraloxime.

## LITERATURE CITED

[1] O. Wallach, Ber. 40, 582 (1907).

[2] W. S. Johnson, E. L. Woroch, and B. G. Buell, J. Am. Chem. Soc. 71, 1901 (1949).

[3] L. Wolff, Lieb. Ann. 322, 351 (1902).

[4] F. M. Beringer and I. Ugelow, J. Am. Chem. Soc., 75, 2635 (1953).

[5] W. Semmler, Ber. 25, 3352 (1892).

[6] H. E. Zaugg, M. Freifelder, and B. W. Horrom, J. Org. Ch. 15, 1197 (1950).

[7] L. C. Cheney and J. R. Piening, J. Am. Chem. Soc. 67, 729 (1945).

[8] A. A. Kotz and Th. Grethe, J. pr. Ch. (2) 80, 473 (1909).

[9] P. A. Berry, A. K. Macbeth and T. B. Swanson, J. Chem. Soc. 1937, 986; R. G. Cooke, A. K Macbeth, J. Chem. Soc. 1937, 1593.

[10] J. A. Hartman, A. J. Tomasewski, and A. S. Dreiding, J. Am. Chem. Soc. 78, 5662 (1956).

[11] G. Schroeter, A. Gluschke, S. Gotzky, J. Huang, G. Irmisch, E. Laves, O. Schrader, and G. Stier, Ber. 63, 1308 (1930).

[12] R. G. Cooke and H. Dowd, Austral. J. Chem. 6, 53 (1953); Referat. Zhur. Khim. 1954, 37763; A. Hardy, E. R. Ward, and L. A. Day, J. Chem. Soc. 1956, 1979.

[13] P. A. Smith, J. Am. Chem. Soc. 70, 325 (1948).

[14] F. Straus and A. Rohrbacher, Ber. 54, 40 (1921).

[15] Nakasaki, J. Chem. Soc. Japan, Pure Chem. Sec. 74, 403 (1953); Referat. Zhur. Khim. 1955, 31601.

[16] G. Theilig, Ber. 86, 96 (1953).

[17] H. Bredereck and R. Compper, Ber. 87, 700 (1954).

[18] O. Michel and E. Grandmougin, Ber. 25, 3431 (1892).

[19] F. Ramirez and A. F. Kirby, J. Am. Chem. Soc. 74, 4331 (1952).

[20] L. Audrieth, and J. Kleinberg, Non-Aqueous Solvent [In Russian] (IL, 1950), p. 169.

[21] T. L. Smith and J. H. Elliot, J. Am. Chem. Soc. 75, 3566 (1953).

[22] F. Straus, O. Bernoully, and P. Mautner, Lieb. Ann. 444, 165 (1925).

[23] F. Ramirez and A. F. Kirby, J. Am. Chem. Soc. 75, 6026 (1953).

[24] W. S. Johnson and H. J. Glenn, J. Am. Chem. Soc. 71, 1092 (1949).

[25] Elseviers Encyclopoedia of Org. Chem., Series III, v. 12B, 2539 (1952).

[26] W. S. Johnson, R. J. Shennan, and R. A. Reed, Organic Reagents for Organic Analysis [In Russian] (IL, 1948), p. 136.

[27] J. V. Braun, Lieb. Ann. 451, 44 (1927).

[28] H. Lindenmann, H. Konitzer, and S. Romanoff, Lieb, Ann. 456, 284 (1927).

[29] N. I. Fischer and F. M. Hamer, J. Chem. Soc. 1934, 962.

[30] R. P. Lastovskii, Technical Analysis in the Manufacture of Dyes and Intermediate Products, Goskhimizdat (1949), p. 180.

[31] Beilst. 6, 627.

[32] C. L. Stevens, J. J. Beereboom, and K. G. Rutherford, J. Am. Chem. Soc. 77, 4590 (1955).

[33] A. L. Wilds and J. A. Johnson, J. Am. Chem. Soc. 68, 86 (1946).

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# THE PROBLEM OF THE REDUCTION OF 1-METHYL-1-CYCLOHEXENE OXIDE

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In 1952 Mousseron and co-workers [1] published the results of the reduction of 1-methyl-1-cyclohexene oxide with lithium aluminum hydride. The only product of this reaction was the tertiary alcohol, 1-methyl-1-cyclohexanol. This work attracted our attention in connection with the study [2] which we were carrying out under the same conditions for the reduction of D-limonene monoxide (1,2-oxido-8(9)-p-menthene). Here, besides the expected tertiary alcohol, β-terpineol, we also obtained the secondary alcohol D-neohydrocarveol with a high degree of asymmetric purity. Both alcohols were formed in almost equal amounts.

Such a course for the reaction was somewhat unexpected when we considered the analogy between 1-methyl-1-cyclohexene oxide and limonene monoxide; this led us to a serious consideration of the data of Mousseron and co-workers. We decided to repeat carefully the reduction of 1-methyl-1-cyclohexene oxide with special attention to the purity of the starting products. To characterize all of the products which we studied we used combination light-scattering spectra.

1-Methyl-1-cyclohexene needed for preparation of the oxide was prepared by dehydration of 1-methyl-1-cyclohexanol with p-toluene sulfonyl chloride in pyridine solution.*. This dehydration process was very successful. The yield of hydrocarbon in this process was 68%. The combination scattering spectrum of this hydrocarbon had a line $\Delta\nu$ 1673 cm$^{-1}$ corresponding to a secondary-tertiary double bond, and no line at $\Delta\nu$ 1655 cm$^{-1}$ [3] which would show the presence in the mixture of the other possible reaction product, methylene cyclohexane. This indicates the assured homogeneity of the 1-methyl-1-cyclohexene which we synthesized. 1-Methyl-1-cyclohexene oxide, prepared by oxidation of this hydrocarbon with peracetic acid, showed properties identical with those of the oxide which was at the disposal of Mousseron and his co-workers.

The results of the reduction of 1-methyl-1-cyclohexene oxide by lithium aluminum hydride fully confirmed their work [1]: the only reduction product was the tertiary alcohol, 1-methyl-1-cyclohexanol. The combination scattering spectrum of this alcohol contained line $\Delta\nu$ 718 cm$^{-1}$, characteristic of the pulsating oscillation of the six-membered ring in tertiary alcohols (as distinct from the secondary alcohols in which this oscillation is characterized by a greater value for $\Delta\nu$ [4]).

## EXPERIMENTAL

Dehydration of 1-methyl-1-cyclohexanol. The original 1-methyl-1-cyclohexanol was obtained from cyclohexanone and methyl magnesium iodide and was characterized by b.p. 76° at 50 mm, m.p. 24-25°, $n_D^{20}$ 1.4611. A mixture of 43.8 g of 1-methyl-1-cyclohexanol, 36 ml of pyridine, and 48.4 g of p-toluene sulfonyl chloride was heated under reflux for 4 hours at an oil bath temperature of 125-130°. After the reaction mixture had cooled it was treated with water and the reaction product was removed with ether. The ether solution was washed with water and dried with potash. The ether was distilled off and the residue fractionated to give 29.7 g (68%) of 1-methyl-1-cyclohexane, b.p. 110-112° at 756 mm and $n_D^{20}$ 1.4503.

Oxidation of 1-methyl-1-cyclohexene. To a solution of 24 g of 1-methyl-1-cyclohexene in 150 ml of ether was gradually added 250 ml of an ether solution of peracetic acid (containing 40 g of $CH_3COOOH$). At the end, the reaction mixture was neutralized with sodium bicarbonate, the ether solution of the resulting oxide was carefully washed with water and dried over potash. After removal of the ether and fractionation we obtained 14.3 g of 1-methyl-1-cyclohexene oxide with b.p. 69-71° at 82 mm, $d_4^{20}$ 0.9327, $n_D^{20}$ 1.4440.

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*Dehydration with p-toluene sulfonyl chloride was used successfully by one of us in 1950 with L. Vinogradova for preparing myrcene from linalool.

Reduction of 1-methyl-1-cyclohexene oxide. A solution of 10 g of the oxide in 125 ml of ether was gradually added in a dry nitrogen atmosphere to 100 ml of an ether solution of lithium aluminum hydride (containing 4.56 g of $LiAlH_4$). After 10 min from the end of the addition of the oxide solution the reaction mixture was cooled with ice and 100 ml of water was gradually added to it. The reaction product was extracted with ether from the liquid part of the mixture. The precipitate was treated with a 25% solution of sodium hydroxide and the resulting solution was also extracted with ether. The combined ether extracts were washed with water and dried with potash. After distillation of the ether and fractionation of the residue we obtained 8.7 g (85%) of the substance with b.p. 64-65° at 23 mm, m.p. 24-25°, and $n_D^{20}$ 1.4611, identical with the starting 1-methyl-1-cyclohexanol.

### Combined Light Scattering Spectra

Spectrum of 1-methyl-1-cyclohexanol, synthesized from cyclohexanone. $\Delta\nu$: 196 (1), 317 (1), 350 (1), 433 (1), 444 (1), 559 (1), 574 (2), 718 (10), 832 (3), 850 (1), 908 (3), 921 (1), 973 (4), 989 (1), 1011 (2), 1039 (3), 1075 (5), 1090 (5), 1120-1178 (8), 1260 (5), 1276 (5), 1344 (2), 1426-1464 (10), 2864 (4), 2928 (7).

Spectrum of 1-methyl-1-cyclohexanol obtained by reduction of 1-methyl-1-cyclohexene oxide. $\Delta\nu$: 169 (1), 319 (1), 355 (1), 398 (1), 431 (1), 454 (2), 574 (3), 687 (?), 718 (10), 832 (5), 849 (2), 911 (3), 928 (1), 973 (4), 1013 (3), 1040 (2), 1074 (5), 1092(5), 1142-1179 (8), 1260 (5), 1275 (5), 1344 (4), 1387 (1), 1430-1461 (10), 2865 (4), 2930 (7).

Spectrum of 1-methyl-1-cyclohexene. $\Delta\nu$: 209 (1), 297 (?), 333 (1), 423 (3), 437 (3), 493 (2), 533 (1), 565 (1), 619 (4), 673 (1), 759 (10), 793 (2), 818 (3), 858 (4), 890 (2), 963 (2), 998 (3), 1022 (1), 1032 (1), 1051 (2), 1069 (3), 1087 (5), 1136 (6), 1153 (6), 1172 (7), 1237 (1), 1267 (5), 1304 (4), 1334 (1), 1349 (4), 1363 (5), 1422-1456 (10), 1673 (10), 2836 (3), 2909 (6), 2934 (6). (Compare with the data of [5]).

Spectrum of 1-methyl-1-cyclohexene oxide. $\Delta\nu$: 378 (1), 408 (1), 474 (1), 492 (1), 533 (1), 558 (3), 670 (10), 759 (8), 812 (1), 822 (1), 885 (1), 910 (2), 969 (2), 997 (1), 1035 (3), 1058 (1), 1080 (1), 1091 (1), 1182 (5), 1218 (2), 1275 (2), 1306 (2), 1348 (2), 1420-1461 (6), 2657 (2), 2910 (4), 2940 (4). (compare with the data of [6]).

## SUMMARY

1. Dehydration of 1-methyl-1-cyclohexanol with p-toluene sulfonyl chloride is a suitable preparative method for obtaining exclusively 1-methyl-1-cyclohexene.

2. The sole product of the reduction of 1-methyl-1-cyclohexene oxide by lithium aluminum hydride is the tertiary alcohol, 1-methyl-1-cyclohexanol. Our data confirm the results obtained by Mousseron and co-workers.

## LITERATURE CITED

[1] M. Mousseron, R. Jaquier, M. Mousseron-Canet, and R. Zagdoun, Bull. Soc. Chim. 1952, 1042

[2] G. V. Pigulevskii, S. A. Kozhin, and V. G. Kostenko, Zh. Obshch. Khim. 28, 1433 (1958).

[3] Hayaschi, Scientific Papers Inst. Phys. Chem. Research, Tokyo. 27, 99 (1935).

[4] G. V. Pigulevskii and S. A. Kozhin, Opt. i. Spektr. 3, 658 (1957).

[5] E. Canals, M. Mousseron, L. Souche, and P. Peyrot, C. r. 202, 1519 (1936).

[6] M. Mousseron and co-workers, Bull. Soc. Chem., 1946, 637.

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# THE FORMATION OF 5-BENZYLHYDANTOIN-3-ACETYLVALINE FROM THE METHYL ESTER OF N-CARBOBENZOXYPHENYLALANYL-GLYCYLVALINE

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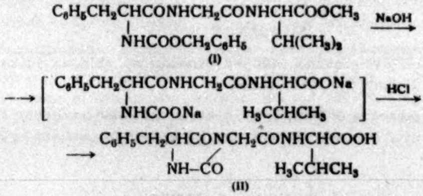
In order to obtain the tripeptide phenylalanylglycylvaline (which was necessary for our further investigations) we prepared the methyl ester of N-carbobenzoxyphenylalanylglycylvaline which was saponified with 1 N sodium hydroxide at 37° under the conditions for saponifying tripeptides [1]. After the solution was acidified with hydrochloric acid and evaporated in a vacuum, besides the expected carbobenzoxyphenylalanylglycylvaline, a white, crystalline substance, melting at 237-240° was isolated. It gave an intense carbonyl reaction with picric acid; the ninhydrin and biuret reactions were negative. After complete hydrolysis with 25% sulfuric acid the substance gave a hydrolyzate which was separated by paper chromatography into phenylalanine, glycine and valine. Reduction of the substance with hydrogen in the presence of Pd black under the conditions for the removal of the carbobenzoxy group did not change it. Analysis and further study of the properties of this substance led to the conclusion that when the methyl ester of carbobenzoxyphenylalanylglycylvaline (I) was saponified by 1 N sodium hydroxide and then acidified and evaporated in a vacuum it formed 5-benzylhydantoin-3-acetylvaline (II). Thus, when the methyl ester of N-carbobenzoxyphenylalanylglycylvaline is saponified, there is simultaneous splitting off of methyl and benzyl alcohols. The unstable carbamic acid of the tripeptide thus formed is transformed into the hydantoin.



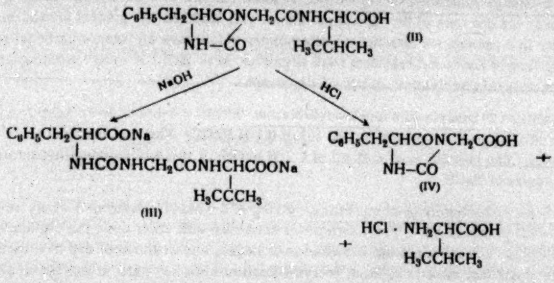
$$\underset{\text{(I)}}{\begin{array}{l}C_6H_5CH_2\overset{}{C}HCONHCH_2CONHCHCOOCH_3\\ \qquad\quad |\qquad\qquad\qquad\qquad |\\ \qquad NHCOOCH_2C_6H_5\quad CH(CH_3)_2\end{array}} \xrightarrow{NaOH}$$

$$\longrightarrow\left[\begin{array}{l}C_6H_5CH_2CHCONHCH_2CONHCHCOONa\\ \qquad\quad |\qquad\qquad\qquad\qquad |\\ \qquad NHCOONa\qquad\quad H_3CCHCH_3\end{array}\right]\xrightarrow{HCl} \qquad (1)$$

$$\longrightarrow \underset{\text{(II)}}{\begin{array}{l}C_6H_5CH_2CHCONCH_2CONHCHCOOH\\ \qquad\quad |\quad\ /\qquad\qquad\quad |\\ \qquad NH{-}CO\qquad\quad H_3CCHCH_3\end{array}}$$

5-Benzylhydantoin-3-acetylvaline dissolves in 0.1 N NaOH with weak heating to combine with 2 moles of alkali. It may be that there occurs opening of the hydantoin ring with formation of the sodium salt of carbonyl bis-phenylalanine-(glycylvaline) (III). When 5-benzylhydantoin-3-acetylvaline is heated with hydrochloric acid (1 : 1), the ring is not broken, but valine is split off and 5-benzylhydantoin-3-acetic acid (IV) is formed.

The formation of hydantoincarboxylic acids from esters of carboalkoxydipeptides has been described in the literature. Thus, Fruton and Bergmann [2] treated the ethyl ester of carbobenzoxy-L-phenylalanylglycine in alcohol solution with ammonia and obtained the amide of 5-benzylhydantoin-3-acetic acid, from which 5-benzylhydantoin-3-acetic acid was isolated by boiling with sulfuric acid. In an analogous way the esters of carbobenzoxyleucylglycine gave the amide of 5-isobutylhydantoin-3-acetic acid [3]. Wessely and co-workers [4] saponified the ester of carbomethyoxyphenylalanylphenylalanine with 1 N sodium hydroxide on the heated water bath and by later acidification of the solution obtained carbonyl bisphenylalanine. Saponification of the esters of carbomethoxyalanylglycine and carbomethoxyglycylalanine under the same conditions gave the identical compound, carbonyl bisglycine (alanine). The authors assumed the formation of hydantoin as an intermediate compound. Earlier, Granacher and Landolt [5] showed the possibility of transforming diamides and esters of carbonyl bisglycine into hydantoin-3-acetic acid by heating on the water bath with hydrochloric acid, and the resulting hydantoin was not destroyed by boiling with hydrochloric acid (1 : 1).



(2)

The formation of 5-benzylhydantoin-3-acetylvaline from the methyl ester of carbobenzoxyphenylalanylglycylvaline thus is in accord with the literature data. However, it is interesting to observe that in the saponification of the methyl ester of carbobenzoxyphenylalanylvalylglycine, which differs in the order of the amino acids, using 1 N sodium hydroxide under the conditions described above, we obtain carbobenzoxyphenylalanylvalylglycine in good yield; the formation of a hydantoin is not found.

## EXPERIMENTAL

Obtaining the methyl ester of N-carbobenzoxyphenylalanylglycylvaline [6]. To 14 g of cbz-phenylalanine* and 7.7 ml of triethylamine in 100 ml anhydrous chloroform cooled to 0° was added 3.5 ml of ethyl chlorocarbonate. After 10 min the reaction mixture was treated in portions with stirring with a cold solution of 10.6 g of methyl glycylvalinate hydrochloride and 6.5 ml of triethylamine in 75 ml of chloroform. The mixture stood 1 hour at 0° and then another hour at 20°. The chloroform solution was washed with 1 N HCl, water, 3% $NaHCO_3$ solution, and again with water, dried over $Na_2SO_4$, and evaporated in a vacuum. A light yellow oil crystallized after treatment with ether. The white crystals, melting at 104°, were easily soluble in methyl and ethyl alcohol. The yield of methyl ester of N-cbz-phenylalanylglycylvaline was 19.1 g (87%).

Found %: N 9.06, 8.88. $C_{25}H_{31}O_6N_3$. Calculated %: N 8.95.

The absorption maximum for the copper complex of the methyl ester of N-cbz-phenylalanylglycylvaline lay in the interval 530-540 mμ.

Saponification of the methyl ester of N-cbz-phenylalanylglycylvaline and formation of 5-benzylhydantoin-3-acetylvaline. 7 g of the methyl ester of N-cbz-phenylalanylglycylvaline was dissolved in 100 ml of methanol. The solution was placed in a thermostat at 37° and treated with 54 ml of 1 N NaOH (at first 30 ml, after 2 hours, 12 ml, then after 1 hour, 6 ml, and at the end of the 4th hour, 6 more ml of 1 N NaOH). Then the solution was diluted with 100 ml of water and acidified to Congo with 5 N HCl. An emulsion formed and was treated with ether. The acid aqueous solution was evaporated in a vacuum to small volume. The white precipitate was filtered, washed with water, and dried. We obtained 4.85 g of substance which after recrystallization from hot water melted at 237-240°. It gave an intense carbonyl reaction with picric acid in soda solution; the ninhydrin and biuret reactions were negative. The yield of 5-benzylhydantoin-3-acetylvaline was 93%.

Found %: C 58.75, 58.93; H 6.16, 6.26; N 12.36, 12.15. $C_{17}H_{21}O_5N_3$. Calculated %: C 58.75; H 6.05; N 12.11.

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*Carbobenzoxy is shortened to cbz.

Hydrolysis of 5-benzylhydantoin-3-acetylvaline. A small amount of 5-benzylhydantoin-3-acetylvaline was hydrolyzed by heating with 25% $H_2SO_4$ in a sealed tube for 10 hours at 135-140°. The neutralized hydrolyzate was submitted to paper chromatography; in an n-butanol-water-acetic acid (4 : 5 : 1) solvent. After the chromatogram was developed with a solution of ninhydrin in n-butyl alcohol it showed three spots, corresponding to phenylalanine, glycine and valine.

Hydrogenation of 5-benzylhydantoin-3-acetylvaline. A small amount of 5-benzylhydantoin-3-acetylvaline was reduced by hydrogen in the presence of Pd black in methanol with addition of glacial acetic acid. After evaporation of the filtrate in a vacuum we obtained a white powder which gave an intense carbonyl reaction with picric acid. The ninhydrin and biuret reactions were negative. M.p. 237°. A mixed melting point with the starting 5-benzylhydantoin-3-acetylvaline showed no depression.

Action of 0.1 N NaOH on 5-benzylhydantoin-3-acetylvaline. 0.0762 g 5-benzylhydantoin-3-acetylvaline was dissolved with slight heating on a water bath in 7.71 ml of 0.1 N NaOH. The excess alkali was titrated with 3.3 ml of 0.1 N $H_2SO_4$. The reaction used 4.41 ml of 0.1 N NaOH; 1 mole of 5-benzylhydantoin-3-acetylvaline combined with 2 moles of NaOH.

Action of HCl on 5-benzylhydantoin-3-acetylvaline. 0.15 g of 5-benzylhydantoin-3-acetylvaline was boiled for 3 hours with 10 ml of HCl (1 : 1). The solution was extracted with ether until the carbonyl reaction vanished in the water solution. The ether extract was dried over $Na_2SO_4$ and evaporated dry in a vacuum. We obtained 0.07 g of white crystalline substance. After recrystallization from hot water it melted at 181-182°. The melting point of 5-benzylhydantoin-3-acetic acid is 181° [5].

A small amount of the substance was hydrolyzed with 25% $H_2SO_4$ for 10 hours at 130-140°. The hydrolyzate was studied by paper partition chromatography; solvent n-butanol-water-acetic acid (4 : 5 : 1). Spots for phenylalanine and glycine were found on the chromatogram.

The acid water solution was evaporated dry in a vacuum. The residue was valine hydrochloride, a white crystalline substance, m.p. 187-189°; according to the literature it melts at 189°. The yield was 0.05 g (100%). Paper chromatography with the same solvent gave only one spot, corresponding to valine.

## SUMMARY

We have described the formation of 5-benzylhydantoin-3-acetylvaline from the methyl ester of N-carbobenzoxyphenylalanylglycylvaline.

## LITERATURE CITED

[1] B. Erlanger, H. Sachs and E. Brand, J. Am. Chem. Soc. 76, 1806 (1954).

[2] J. Fruton and M. Bergmann, J. Biol. Ch. 145, 253 (1942).

[3] C. Dekker, S. Taylor and J. Fruton, J. Biol. Ch. 180, 155 (1949).

[4] F. Wessely, E. Kenn and J. Mayer, Z. physiol. Ch. 180, 64 (1929).

[5] C. Granacher and H. Landolt, Helv. Chim. Acta 10, 799 (1927).

[6] R. A. Boissonnas, Helv. Chim. Acta 34, 874 (1951).

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# THE SYNTHESIS OF CYANOMETHYL ESTERS OF PEPTIDES AND THEIR USE IN OBTAINING PEPTIDES

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Recently Schwyzer and co-workers have presented a new method for the synthesis of peptides. They studied a whole series of activated esters of hippuric acid in the reaction with benzylamine and found the most reactive acylating agents to be the cyanomethyl esters [1]. In later communications [2-5] these authors studied the possibility of using the cyanomethyl esters in the synthesis of peptides in more complex models. They showed that the cyanomethyl esters of amino acid and peptide derivatives were easily obtained, could be isolated in crystalline form, were sufficiently active and stable, and offered the possibility of carrying out the synthesis of peptides at room temperature. The use of the cyanomethyl esters of peptides for obtaining cyclopeptides was especially interesting [6].

In the present work we have obtained the cyanomethyl esters of some carbobenzoxy derivatives of amino acids, dipeptides, and tripeptides, and studied their usefulness in the synthesis of peptides and their stability when the carbobenzoxy group was removed by hydrogen bromide in glacial acetic acid.

The cyanomethyl esters were obtained by reaction of cbz-amino acids * or cbz-peptides with chloroacetonitrile in the presence of triethylamine with heating to 60-70°. The canomethyl esters were prepared from: cbz-phenylalanine, cbz-phenylalanylglycine, cbz-phenylalanylglycylleucine, cbz-glycylphenylalanine, cbz-glycylphenylalanylleucine, cbz-glycylleucylphenylalanine. The results of the experiments are given in Table 1.

TABLE 1

| Cyanomethyl ester of the compounds | Formula | Yield % | Melting point |
|---|---|---|---|
| cbz-Phenylalanine | $C_{19}H_{18}O_4N_2$ | 80.9 | 98—99° |
| cbz-Phenylalanylglycine | $C_{21}H_{21}O_5N_3$ | 72.0 | 100—101 |
| cbz-Glycylphenylalanine | $C_{21}H_{21}O_5N_3$ | 84.7 | 70—72 |
| cbz-Phenylalanylglycylleucine | $C_{27}H_{32}O_6N_4$ | 65.2 | 113—114 |
| cbz-Glycylphenylalanylleucine | $C_{27}H_{32}O_6N_4$ | 78.1 | 110—111 |
| cbz-Glycylleucylphenylalanine | $C_{27}H_{32}O_6N_4$ | 74.8 | 127—129 |

As these data show, the cyanomethyl esters of the carbobenzoxy derivatives of peptides are obtained in good yield and in the crystalline state.

The synthesis of peptides by the use of the cyanomethyl esters of carbobenzoxy amino acids or peptides proceeds in anhydrous chloroform in the reaction with the methyl esters of amino acid or peptide hydrochlorides

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* Carbobenzoxy is shortened to cbz.

in the presence of triethylamine and small amounts of glacial acetic acid. Below we give comparative data on the synthesis of peptides using cyanomethyl esters and using the method of Boissonnas through mixed anhydrides of cbz-amino acids and ethyl carbonate combined with the methyl esters of the hydrochlorides of amino acids or peptides in the presence of triethylamine (Table 2).

TABLE 2

| Reacting compounds | | Peptides obtained | | |
|---|---|---|---|---|
| I | II | Name | Yield, % | Melting point |
| Cyanomethyl ester of cbz-phenylalanine | Methyl glycinate hydrochloride | Methyl ester of cbz-phenylalanylglycine | 79.0 | 114-115° |
| cbz-Phenylalanine | The same | The same | 78.3 | 114-115 |
| Cyanomethyl ester of cbz-phenylalanine | Methyl glycylleucinate hydrochloride | Methyl ester of cbz-phenylalanylglycylleucine | 50.0 | 114-118 |
| cbz-Phenylalanylglycine | Methyl leucinate hydrochloride | The same | 76.2 | 117-118 |
| Cyanomethyl ester of cbz-glycine | Methyl phenylalaninate hydrochloride | Methyl ester of cbz-glycylphenylalanine | 85.0 | 80-82 |
| cbz-Glycine | Methyl leucinate hydrochloride | Methyl ester of cbz-glycylleucine | 88.6 | - |
| cbz-Glycylphenylalanine | The same | Methyl ester of cbz-glycylphenylalanylleucine | 63.9 | 93-95 |
| cbz-Glycylleucine | Methyl phenylalaninate hydrochloride | Methyl ester of cbz-glycylleucylphenylalanine | 55.3 | 118-120 |

The results show that the method of cyanomethyl esters can be used for the synthesis of peptides just as can the widely used method of Boissonnas.

In the present work we present experiments on the removal of the carbobenzoxy group in the cyanomethyl esters of cbz-tripeptides by the action of hydrogen bromide in glacial acetic acid (Table 3).

TABLE 3

| Cyanomethyl ester of tripeptide hydrobromide | Formula | % yield | Melting point |
|---|---|---|---|
| Cyanomethyl ester of phenylalanylglycylleucine hydrobromide | $C_{19}H_{27}O_4N_4Br$ | 89.4 | 192-193° (decomp) |
| Cyanomethyl ester of glycylphenylalanylleucine hydrobromide | $C_{19}H_{27}O_4N_4Br \cdot 6H_2O$ | 86.4 | - |
| Cyanomethyl ester of glycylleucylphenylalanine hydrobromide | $C_{19}H_{27}O_4N_4Br$ | 61.5 | 197-198° (decomp) |

The resulting cyanomethyl esters of tripeptide hydrobromides were hygroscopic and contained water of crystallization. In the case of the cyanomethyl ester of glycylphenylalanylleucine hydrobromide the water could not be removed after prolonged drying over $P_2O_5$ in a vacuum at 60°.

Cyanomethyl ester of cbz-phenylalanine. 7.5 g of cbz-phenylalanine was mixed with 5.25 ml of triethylamine and 4.75 ml of chloroacetonitrile. The resulting viscous mass was heated for one half hour to 70° on a water bath and then allowed to stand overnight at 20°. Then the reaction mixture was treated with ethyl acetate. The resulting precipitate of trimethylamine hydrochloride was filtered off and the ethyl acetate solution was washed with dilute HCl, a 3% solution of $NaHCO_3$, and water, dried over ignited $Na_2SO_4$, and evaporated in a vacuum. The remaining oil crystallized when absolute ether was added. We obtained 6.8 g of the cyanomethyl ester of cbz-phenylalanine. After reprecipitation from aqueous methanol it melted at 98-99°.

Found %: N 8.34, 8.27. $C_{19}H_{18}O_4N_2$. Calculated %: N 8.28.

Methyl ester of cbz-phenylalanylglycine. A) A solution of 15 g of the cyanomethyl ester of cbz-phenylalanine in 100 ml of anhydrous chloroform was treated with 8.3 g of methyl glycinate hydrochloride, 18.3 ml of triethylamine, and 0.29 ml of glacial acetic acid. After standing for 64 hours at 20°, the solution was washed with dilute HCl, water, 3% $NaHCO_3$, water, dried over $Na_2SO_4$, and evaporated in a vacuum. The remaining oil crystallized when it stood with ether. We obtained 12.4 g of the methyl ester of cbz-phenylalanylglycine.

B) The methyl ester of cbz-phenylalanylglycine was obtained by the method of Boissonnas: a solution of 7.5 g of cbz-phenylalanine and 3.9 g triethylamine in 75 ml of anhydrous chloroform was cooled to −5° and 2.7 ml of ethyl chlorocarbonate awas added. After 10 min the reaction mixture was treated with a cooled solution of 3.55 g of methyl glycinate hydrochloride and 3.9 ml of triethylamine in 100 ml of anhydrous chloroform in portions with stirring. The reaction mixture stood for 1 hour in an ice bath and then was kept for 2 hours at 20°. After washing the solution with dilute HCl, water, 3% $NaHCO_3$, and again water, it was dried over $Na_2SO_4$ and evaporated in a vacuum to give 7.25 g of the methyl ester of cbz-phenylalanylglycine. After drying over $P_2O_5$ at 10 mm the compound melted at 114-115°.

Found %: N 7.61. $C_{20}H_{22}O_5N_2$. Calculated %: N 7.56.

cbz-Phenylalanylglycine. A suspension of 4.6 g of the methyl ester of cbz-phenylalanylglycine in 50 ml of methanol and 7.4 ml of 2 N NaOH was shaken for 1 hour at 20°. The solution was diluted with water and acidified with 5 N HCl to Congo. We obtained 4 g (90.9%) of cbz-phenylalanylglycine, m.p. 154-155°.

Found : equiv. 351.3. $C_{19}H_{20}O_5N_2$. Calculated: equiv. 356.

Cyanomethyl ester of cbz-phenylalanylglycine. A mixture of 1.38 g of cbz-phenylalanylglycine, 0.79 g of triethylamine, and 0.71 ml of chloroacetonitrile was kept at 60° and treated in the usual way (cf. cyanomethyl ester of cbz-phenylalanine). We obtained 1.08 g of the cyanomethyl ester of cbz-phenylalanylglycine.

Found %: N 10.55, 10.47. $C_{21}H_{21}O_5N_3$. Calculated %: N 10.63.

Methyl ester of cbz-phenylalanylglycylleucine. A) To a solution of 3.15 g of the canomethyl ester of cbz-phenylalanine in 50 ml of anhydrous chloroform was added 3.5 g of the methyl ester of glycylleucine hydrochloride, 3.9 ml of triethylamine, and 0.06 ml of glacial acetic acid. The reaction mixture stood at 20° for 72 hours. The solution was treated in the usual way. After removal of the solvent in a vacuum, an oil remained and crystallized when it stood with anhydrous ether. We obtained 2.25 g of the methyl ester of cbz-phenylalanylglycylleucine.

B) Using the Boissonnas method we combined 9.77 g cbz-phenylalanylglycine and 5.7 g of methyl leucinate hydrochloride in 170 ml of anhydrous chloroform in the presence of 8.7 ml of triethylamine and 3 ml of ethyl chlorocarbonate to obtain 10.06 g of the methyl ester of cbz-phenylalanylglycylleucine.

Found %: N 8.73, 8.40. $C_{26}H_{33}O_6N_3$. Calculated %: N 8.68.

cbz-Phenylalanylglycylleucine. A suspension of 5.9 g of the methyl ester of cbz-phenylalanylglycylleucine in 7.3 ml of 2 N NaOH and 50 ml of methanol was kept for 10 hours at 20°. At the end of the 10th hour the solution was increased by 1.5 ml more of 2 N NaCH, and then the solution was diluted with water and acidified with 5 N HCl. The oil which precipitated was extracted with ether, the ether solution was dried over $Na_2SO_4$ and evaporated in a vacuum. An oil remained which was dissolved in a minimum amount of methanol and was precipitated by water. We obtained 4.48 g (78.3%) of cbz-phenylalanylglycylleucine, m.p. 74-75°.

Found %: C 63.68, 63.54; H 6.97, 6.81. $C_{25}H_{31}O_6N_3$. Calculated %: C 63.96; H 6.61.

Cyanomethyl ester of cbz-phenylalanylglycylleucine. A mixture of 3 g of cbz-phenylalanylglycylleucine, 1.3 ml of triethylamine and 1.2 ml of chloroacetonitrile was heated for 4 hours on the water bath at 70° and then stood overnight at 20°. After the usual treatment we obtained an oil which crystallized in ether. The yield of cyanomethyl ester of cbz-phenylalanylglycylleucine was 2.12 g.

Found %: N 11.07, 10.75. $C_{27}H_{32}O_6N_4$. Calculated %: N 11.02.

Cyanomethyl ester of pnehylalanylglycylleucine hydrobromide. To 2 g of the cyanomethyl ester of cbz-phenylanylglycylleucine was added 2.8 ml of glacial acetic acid saturated with HBr. After an hour (at the end of evolution of bubbles of $CO_2$) the reaction mixture had the appearance of a yellow oil and 100 ml of anhydrous ether was added to it. When the oil was stirred with the ether, it crystallized. After three reprecipitations by ether from anhydrous methanol, 1.52 g of the cyanomethyl ester of phenylalanylglycylleucine hydrobromide was obtained. The compound gave a positive hydroxamic reaction; its nature was confirmed by paper chromatography. The hydrobromide was hygroscopic, although it did not deliquesce in air.

Found %: N 11.83, 11.73. $C_{19}H_{27}O_4N_4Br \cdot H_2O$. Calculated %: N 11.83.

The substance was dried for a week over $P_2O_5$ at 10 mm and 60°.

Found %: N 12.2, 12.39. $C_{19}H_{27}O_4N_4Br$. Calculated %: N 12.3.

Methyl ester of cbz-glycylphenylalanine. 5 g of cyanomethyl ester of cbz-glycine [2] was dissolved in 40 ml of anhyrous chloroform. To the solution was added 5.2 g of methyl phenylalaninate hydrochloride, 4.30 ml of triethylamine, and 0.13 ml of glacial acetic acid. The reaction mixture stood at 20° for 50 hours. After the usual treatment we obtained an oil which crystallized when it stood with anhydrous ether. The methyl ester of cbz-glycylphenylalanine was obtained in the form of white silky needles.

Found %: N 7.73, 7.40. $C_{20}H_{22}O_5N_2$. Calculated %: N 7.56.

cbz-Glycylphenylalanine. To a suspension of 3.7 g of the methyl ester of cbz-glycylphenylalanine in 40 ml of methanol was added 6 ml of 2 N NaOH. The reaction mixture stood for an hour at 20°. The clear solution was diluted with water and acidified with 0.72 ml of glacial acetic acid. The white, crystalline precipitate was filtered, washed with water, and dried in a vacuum desiccator over $H_2SO_4$. We obtained 3 g (84.2%) of cbz-glycylphenylalanine, m.p. 155-156°.

Found: equiv. 356. $C_{19}H_{20}O_5N_2$. Calculated: equiv. 356.

Cyanomethyl ester of cbz-glycylphenylalanine. A mixture of 1.1 g of cbz-glycylphenylalanine, 0.56 ml of chloroacetonitrile, and 0.62 ml of triethylamine was heated at 60° for 2 hours and then stood overnight at 20°. After the usual treatment we obtained 1 g of cyanomethyl ester of cbz-glycylphenylalanine.

Found %: N 10.76, 10.83. $C_{21}H_{21}O_5N_3$. Calculated %: CN 10.63.

Methyl ester of cbz-glycylphenylalanylleucine. 5.6 g of cbz-glycylphenylalanine was combined by the Boissonnas method with 3.3 g of methyl leucinate hydrochloride in 150 ml of anhydrous chloroform in the presence of 5 ml of triethylamine and 1.7 ml of ethyl chlorocarbonate with cooling. After the usual treatment we obtained 4.85 g of the methyl ester of cbz-glycylphenylalanylleucine.

Found %: N 8.90, 8.90. $C_{26}H_{33}O_6N_3$. Calculated %: N 8.69.

cbz-Glycylphenylalanylleucine. A mixture of 4.3 g of methyl ester of cbz-glycylphenylalanylleucine and 5.3 ml of 2 N NaOH in 35 ml of methanol was kept for 5 hours at 20°. The clear solution was treated with water and acidified with 5 N HCl to Congo. We obtained 3.52 g (85.8%) of cbz-glycylphenylalanylleucine, m.p. 140-141°.

Found: equiv. 470. $C_{25}H_{31}O_6N_3$. Calculated: equiv. 469.

Cyanomethyl ester of cbz-glycylphenylalanylleucine. A mixture of 3.37 g of cbz-glycylphenylalanylleucine, 1.46 ml of triethylamine, and 1.33 ml of chloroacetonitrile stood 36 hours at 20° and then was heated

3 hours at 60 – 70° and treated in the usual way. We obtained an oil which crystallized in ether. The yield of cyanomethyl ester of cbz-glycylphenylalanylleucine was 2.82 g. After reprecipitation from aqueous methanol and drying in a vacuum desiccator over $H_2SO_4$, it melted at 110-111°.

Found %: N 11.01. $C_{27}H_{32}O_6N_4$. Calculated %: N 11.02.

Cyanomethyl ester of glycylphenylalanylleucine hydrobromide. 2.4 g of cyanomethyl ester of cbz-glycylphenylalanylleucine was treated with 3.4 ml of glacial acetic acid saturated with HBr. After 2.5 hours (at the end of evolution of $CO_2$) the reaction mixture was treated with 100 ml of anhydrous ether and the mixture stood overnight in the cold (–10°). The oil which precipitated was washed free of excess HBr by repeated reprecipitations from methanol with anhydrous ether. Then the oil was dissolved in 10 ml of water, the solution was extracted with ether, and evaporated to dryness in a vacuum. The colorless oil which remained was treated several times with ethyl alcohol and acetone. After removal of the solvents in a vacuum there remained a white, amorphous substance which quickly deliquesced in air. The homogeneity of the cyanomethyl ester of glycylphenylalanylleucine hydrobromide which we obtained was shown by paper chromatography. The hydroxamic reaction was positive. Yield 1.85 g.

Found %: N 9.56, 9.62. After repeated drying over $P_2O_5$ at 10 mm and 60° and analytical data were almost unchanged.

Found %: N 9.79, 9.70. $C_{19}H_{27}O_4N_4Br \cdot 6H_2O$. Calculated %: N 9.94.

Methyl ester of cbz-glycylleucine. 10.45 g cbz-glycine was combined by the Boissonnas method with 9.1 g methyl leucinate hydrochloride in 150 ml of chloroform in the presence of 15.2 ml of triethylamine and 5.7 ml of ethyl chlorocarbonate with cooling. The reaction mixture was kept for 1 hour in an ice bath, then for 2 hours at 20° and then was treated in the usual way. We obtained a colorless oil. The yield of methyl ester of cbz-glycylleucine was 14.87 g.

Found %: N 8.21, 8.07. $C_{17}H_{24}O_5N_2$. Calculated %: C 8.33.

cbz-Glycylleucine. 10.08 g methyl ester of cbz-glycylleucine was dissolved in 150 ml of anhydrous methanol and to the solution was added 44 ml of 1 N NaOH. After 30 min the clear solution was acidified with 5 N HCl to Congo, and diluted with water to full precipitation of cbz-glycylleucine. We obtained 7.1 g (73.5%) of substance melting at 123-124°.

Found: equiv. 323, 315. $C_{16}H_{22}O_5N_2$. Calculated: equiv. 322.

Methyl ester of cbz-glycylleucylphenylalanine. 9.45 g of cbz-glycylleucine and 6.15 g of methyl phenylalaninate hydrochloride were combined by the Boissonnas method in the presence of 8.8 ml of triethylamine and 125 ml of anhydrous chloroform with 3.23 ml of ethyl chlorocarbonate with cooling. After the usual treatment we obtained 7.75 g of methyl ester of cbz-glycylleucylphenylalanine. After reprecipitation from methanol by water it melted at 118-120°.

Found %: N 8.79, 8.54. $C_{26}H_{33}O_6N_3$. Calculated %: N 8.69.

cbz-Glycylleucylphenylalanine. 7.75 g of the methyl ester of cbz-glycylleucylphenylalanine was shaken for 1 hour with 9.6 ml of 2 N NaOH in 65 ml of methanol at 20°. The solution stood another hour at 20° and then was diluted with water and acidified with 5 N HCl. We obtained 7 g (93.3%) cbz-glycylleucylphenylalanine with m.p. 152-154°.

Found: equiv. 472. $C_{25}H_{31}O_6N_3$. Calculated: equiv. 469.

Cyanomethyl ester of cbz-glycylleucylphenylalanine. A mixture of 1.2 of cbz-glycylleucylphenylalanine, 0.52 ml of triethylamine, and 0.47 ml of chloroacetonitrile was kept for 12 hours at 20°, then was heated for 2 hours at 70°. After the usual treatment we obtained 0.95 g of cyanomethyl ester of cbz-glycylleucylphenylalanine with m.p. 107-122°. After reprecipitation from methanol by water the compound melted at 127-129°.

Found %: N 11.09, 10.91. $C_{27}H_{32}O_6N_4$. Calculated %: N 11.02.

Cyanomethyl ester of glycylleucylphenylalanine hydrobromide. 2.1 g of cyanomethyl ester of cbz-glycylleucylphenylalanine was treated with 2.1 ml of acetic acid saturated with HBr, and kept 30 min at 20°.

Then to the mixture was added 10 ml of anhydrous methanol and after 20 min, 100 ml of anhydrous ether. A yellow oil precipitated. After twice reprecipitating from alcohol by ether we obtained 1.15 g of cyanomethyl ester of glycylleucylphenylalanine hydrobromide. The homogeneity of the compound was shown by paper chromatography. The hydroxamic reaction was positive.

Found %: N 11.30, 11.19. $C_{19}H_{27}O_4N_4Br \cdot 2H_2O$. Calculated %: N 11.40.

The substance was dried over $P_2O_5$ at 10 mm and 60°.

Found %: N 12.35. $C_{19}H_{27}O_5Br$. Calculated %: N 12.30.

## SUMMARY

We have described the synthesis of cyanomethyl esters of carbobenzoxy derivatives of peptides and their use in preparing peptides. We have synthesized cyanomethyl esters of: carbobenzoxyphenylalanine, carbobenzoxyphenylalanylglycine, carbobenzoxyglycylphenylalanine, carbobenzoxyphenylalanylglycylleucine, carbobenzoxyglycylphenylalanylleucine, and carbobenzoxyglycylleucylphenylalanine.

We have obtained the peptide derivatives: methyl ester of carbobenzoxyphenylalanylglycine, methyl ester of carbobenzoxyglycylphenylalanine, methyl ester of carbobenzoxyglycylleucine, and methyl ester of carbobenzoxyphenylalanylglycylleucine.

We have isolated the hydrobromides of the cyanomethyl esters of the tripeptides: phenylalanylglycylleucine, glycylphenylalanylleucine, and glycylleucylphenylalanine.

## LITERATURE CITED

[1] R. Schwyzer, B. Iselin and M. Feurer, Helv. Chim. Acta 38, 69 (1955).

[2] R. Schwyzer, M. Feurer, B. Iselin and H. Kagi, Helv. Chim. Acta 38, 80 (1955).

[3] R. Schwyzer, M. Feurer and B. Iselin, Helv. Chim. Acta 38, 83 (1955).

[4] R. Schwyzer and B. Iselin, Ann. Acad. Sci. Fennica, AII 60, 181 (1955).

[5] B. Iselin, M. Feurer and R. Schwyzer, Helv. Chim. Acta 38, 1508 (1955).

[6] R. Schwyzer, B. Iselin, W. Rittel and P. Sieber, Helv. Chim. Acta 39, 872 (1956).

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# STUDIES IN THE FIELD OF THE CHEMISTRY OF THE CYANINE DYES

## XIII. * THIACYANINES WHICH CONTAIN UNSATURATED RADICALS AS SUBSTITUENTS IN THE 6,6'-POSITIONS OF BENZTHIAZOLE

I. K. Ushenko and S. E. Gornostaeva

In the present communication we describe the synthesis of thiacarbocyanines which contain, in the 6,6'-positions of the benzthiazole, unsaturated radicals (styryl, p-methoxystyryl, and α-thienylvinyl). It is assumed that the introduction of unsaturated radicals into the benzthiazole nucleus of the dyes will lengthen the chromophore and deepen the color of the thiacarbocyanine. Cyanine dyes of this type have not been known before.

The synthesis of the starting bases was carried out by the Meerwein reaction, by the action of diazotized 2-methyl-6-aminobenzthiazole on unsaturated acids.

In the reaction of aryl diazonium halides with α,β-unsaturated carbonyl compounds, Meerwein [1] obtained α-halo-β-arylalkanes or alkenes. The reaction goes in a water-acetone solution in the presence of catalytic amounts of cupric chloride. The large number of unsaturated compounds which were introduced into this reaction could be assigned to the classes: simple ethylenes [2,7], aromatic ethylenes [3], α,β-unsaturated carbonyl compounds [4], cinnamic acid and its derivatives [1, 5], coumarins [1], acrylic acid [6], acrylonitrile [4, 8, 9], acetylenes [1, 2], dienes with conjugated bonds [10], and benzoylacrylic acid [11].

The mechanism of this interesting reaction was the subject of much discussion [8, 9, 12]. The discussion centered around two points: 1) the character of the reaction (homolytic or heterolytic), 2) the role of the divalent copper and the specificity of the acetone in this reaction. Recently Kochi has published some work [13] in which he gives a mechanism and the kinetics of the Meerwein reaction. Kochi showed that the Meerwein reaction could proceed also in a water-alcohol solution, but the yield of arylation products was considerably lower. Attempts to carry out the Meerwein reaction in the absence of copper salts in a water-acetone solution were unsuccessful [8].

Heterocyclic diazo compounds until now have not been introduced into reaction with unsaturated compounds. We were concerned with this type of investigation, and first we took an amine of the benzthiazole series, 2-methyl-6-aminobenzthiazole. In the reaction of diazotized 2-methyl-6-aminobenzthiazole with cinnamic, p-methoxycinnamic, and α-thienylacrylic acids under the conditions of the Meerwein reaction, we succeeded in obtaining three new basic derivatives of 2-methyl-benzthiazole which contained unsaturated substituents in the 6-position.

At the time when we carried out the reaction we observed the evolution of nitrogen and carbon dioxide. Among the reaction products, aside from benzthiazoles with unsaturated radicals, we observed 2-methyl-6-chlorobenzthiazole, chloroacetone, and azo compounds.

The synthesis of 2-methyl-6-styrylbenzthiazole could be presented thus:

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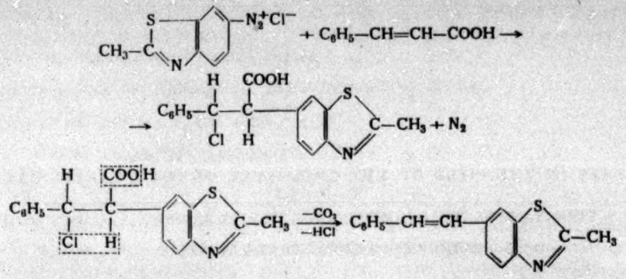
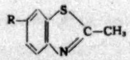
*Communication XII in Ukrain. Khim. Zhur. 22, 76 (1956).

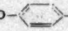


2-Methyl-6-styrylbenzthiazole was also obtained by reaction of styrene with benzthiazolene diazonium chloride. The yield did not exceed 3-4%.

Table 1 gives the new bases which we synthesized.

TABLE 1



| R | % Yield of basic product | Melting point of basic product | Yield of byproducts (in g) |  | Amount of unreacted acrylic acid |
|---|---|---|---|---|---|
|  |  |  | chloroacetone | 2-methyl-6-chlorobenzthiazole |  |
| $C_6H_5-CH=CH-$ | 17 | 118° | 2 | 2.3 | 1.7 |
| $CH_3O-$$-CH=CH-$ | 6.8 | 170—171 | — | 1.2 | 7 |
| $-CH=CH-$ | 9.5 | 119—120 | — | 0.3 | 2.2 |

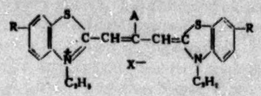
The low yield of benzthiazole which contains unsaturated groups in position 6 can be explained by the fact that a number of side reactions occur.

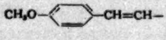
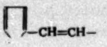
The amount of unreacted acid depends strongly on its solubility in acetone. The poorer the solubility of the acid in acetone, the less the yield of styryl benzthiazole. In order to reduce the side reactions to a minimum we had to observe a number of conditions, chiefly reaction temperature and acidity of the solution. The activity of the unsaturated compounds used in the reaction was also very important.

When the bases were heated with dimethyl or diethyl sulfate, decomposition products were formed along with the quaternary salts. Therefore the quaternary salts were obtained by heating the bases with methyl or ethyl p-toluenesulfonate. When the quaternary salts were condensed with orthoesters we obtained thiacarbocyanines which are shown in Table 2. For comparison we also give 3,3'-diethylthiacarbocyanine.

Table 2 shows that the introduction of unsaturated substituents in the 6,6'-positions of thiacarbocyanines sharply changes the absorption maxima in the long wave portion of the spectrum (by 37-47 mμ). The introduction of the methoxy group in the position para to the styryl radical causes a further shift in the absorption spectrum of the long wave portion by 10 mμ. Thus the effect of the p-methoxystyryl and the α-thienylvinyl radical on the color is almost the same.

TABLE 2

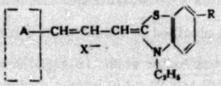


| Compound No. | R | A | Absorption maximum (in mμ) |
|---|---|---|---|
|  | H | H | 558 |
| (I) | $C_6H_5$—CH=CH— | H | 595 |
| (II) |  | $CH_3$ | 580 |
| (III) |  | $C_2H_5$ | 585 |
| (IV) |  | H | 605 |
| (V) |  | $C_2H_5$ | 596 |
| (VI) |  | H | 606 |
| (VII) |  | $C_2H_5$ | 598 |

Quaternary salts were also produced by condensation with the ethyl p-toluenesulfonate of 2-(β-acetanilidovinyl)-4,5-benzobenzthiazole and 2-(β-acetanilidovinyl)-5-methoxybenzthiazole, from which we obtained five unsymmetrical thiacarbocyanines, shown in Table 3.

Besides these we also obtained three rhodacyanines which are shown in Table 4.

TABLE 3



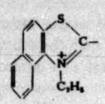
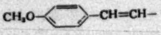
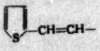
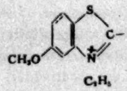
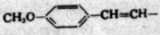
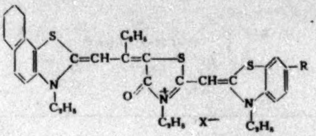
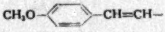
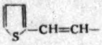
| Compound No. | A | R | Absorption maximum (in mμ) |
|---|---|---|---|
|  |  | H | 581 |
| (VIII) |  | $C_6H_5$—CH=CH— | 596 |
| (IX) |  |  | 601 |
| (X) |  |  | 600 |
| (XI) |  | $C_6H_5$—CH=CH— | 589 |
| (XII) |  |  | 595 |

TABLE 4



| Compound No. | R | Absorption maximum (in mμ) |
|---|---|---|
| | H | 612 |
| (XIII) | $C_6H_5-CH=CH-$ | 627 |
| (XIV) |  | 631 |
| (XV) |  | 633 |

From the results in Tables 3 and 4 it is evident that in unsymmetrical cyanine dyes the introduction of unsaturated groups in position 6 of the benzthiazole ring also causes a considerable shift of the absorption maximum in the long wave portion of the spectrum.

## EXPERIMENTAL

α-Thiophene aldehyde was obtained from thiophene, N-ethyl formanilide, and phosphorus oxychloride [14, 15].

2-Thienylacrylic acid was prepared from α-thiophene aldehyde and malonic acid [16].

p-Methoxy cinnamic acid was obtained from anisaldehyde and malonic acid [17].

2-Methyl-6-aminobenzthiazole was obtained by reduction of 2-methyl-6-nitrobenzthiazole.

2-Methyl-6-styrylbenzthiazole from cinnamic acid. 16.4 g of 2-methyl-6-aminobenzthiazole was dissolved in 25 ml of hydrochloric acid (d 1.19) and 20 ml of water. The solution was cooled to −5° and diazotized with 7.5 g of sodium nitrite in 12 ml of water. At the same time a three-necked flask was fitted with a thermometer, stirrer, and stopper, and in it was placed a mixture of 14.8 g of cinnamic acid, 120 ml of acetone, 24 g of crystalline sodium acetate, and 5.1 g of cupric chloride ($CuCl_2 \cdot 2H_2O$) in 10 ml of water. The mixture was cooled to −5°, and to the resulting suspension with stirring was added the prepared solution of diazonium chloride over a period of 30 min. The flask was then connected with a Tishchenko flask with a barium hydroxide solution. The mixture was stirred at −2° for 2 hours, and then for 4-5 hours more during which the temperature gradually rose to that of the room. At −2° slow evolution of a gaseous product began, at 0° this became intense, and after some time a copious precipitate of barium carbonate appeared in the Tishchenko flask. On the next day the mixture was steam distilled, the acetone was collected separately, and the residual distillate (about 2 liters) was redistilled until the last portion of the distillate contained no halogen. The acetone fraction was redistilled in a column and yielded 2 g of chloroacetone. The water distillate gave 2.3 g of 2-methyl-6-chlorobenzthiazole, m.p. 79-80°. Cinnamic acid which precipitated in the distillation flask when it cooled, was separated from the brown mass which was dissolved in chloroform and the solution chromatographed on aluminum oxide. The eluate from the first zone (light yellow in color) was collected separately, and the chloroform was completely distilled from it. It gave 4.5 g of base. The eluate from the second zone (dark brown in color) was partly freed from chloroform by distillation; the solution was repeatedly chromographed. It yielded 2.7 g of base. The total yield was 7.2 g (28%), m.p. 109-111°. The base was recrystallized twice from alcohol using animal charcoal. Yield 4.3 g (17%). Light-yellow plates with a pearly luster; m.p. 118°.

Found %: S 13.01, 13.03; N 5.50, 5.76. $C_{16}H_{13}NS$. Calculated %: S 12.71; N 5.57.

2-Methyl-6-styrylbenzthiazole from styrene. 8.2 g 2-methyl-6-aminobenzthiazole was diazotized as described above. A mixture of 5.5 g of styrene (stabilized with 0.5% hydroquinone), 50 ml of acetone, and 15.3 g of sodium acetate was cooled to −2°. To the mixture was added the diazonium chloride solution and 1 g of cupric chloride in 3 ml of water. Stirring continued for 2 hours during which time the temperature was raised to 35° and then the mixture was stirred for another 3 hours at 35°. The solution was filtered, the acetone layer was separated, and the acetone was distilled with steam. To the residue was added 40 g of potassium hydroxide in 100 ml of alcohol, and the mixture was boiled for 2 hours. Then the solution was steam distilled to remove 2-methyl-6-chlorobenzthiazole and unreacted styrene. The residual dark mass was extracted with chloroform and the solution was chromatographed on aluminum oxide. We obtained light-yellow crystals which were recrystallized from alcohol. The yield was 0.5 g (4%), m.p. 118°. The mixed melting point with the 2-methyl-6-styrylbenzthiazole described above gave no depression.

2-Methyl-6-(p-methoxystyryl)-benzthiazole. 16.4 g of 2-methyl-6-aminobenzthiazole was diazotized in the usual way. A mixture of 17.8 g p-methoxycinnamic acid, 200 ml of acetone, 24 g of sodium acetate, and 5.1 g of cupric chloride in 10 ml of water was cooled to −7° and the solution of diazonium chloride was added to it during 40-45 min. The reaction mixture was stirred 5-6 hours while the temperature was slowly raised to 20°; acetone and 2-methyl-6-chlorobenzthiazole (1.2 g) were distilled off with steam. After decantation of the water solution, from which as it cooled, had precipitated 1.5 g of p-methoxycinnamic acid, we obtained 29.4 g of a dark brown residue. The product was ground and dissolved in 400-500 ml of chloroform, from which cooling precipitated 5.5 g of p-methoxycinnamic acid. The chloroform was partly distilled off and the residue was submitted to chromatography. We obtained 2.4 g of red-brown substance which was twice recrystallized from alcohol with animal charcoal. Yield 1.9 g (6.8%). Silvery scales with a greenish tint; m.p. 170-171°. The yield based on reacting p-methoxycinnamic acid was 11.1%.

Found %: N 5.19, 5.32; S 11.34, 11.45. $C_{17}H_{15}ONS$. Calculated %: N 4.98; S 11.39.

2-Methyl-6-(α-thienylvinyl)-benzthiazole. 16.4 g of 2-methyl-6-aminobenzthiazole was diazotized as described above. A mixture was prepared of 15.4 g 2-thienylacrylic acid, 250 ml of acetone, 24 g of sodium acetate, and 5.1 g of cupric chloride in 10 ml of water. Addition of diazonium chloride and stirring were carried out as above. The acetone and 2-methyl-6-chlorobenzthiazole (0.3 g) were steam-distilled as above. From the distillation flask after decantation of the water layer we obtained 30.4 g of dark product and 2.2 g of thienylacrylic acid. The product was ground, dissolved in 500 ml of chloroform, filtered, the solution concentrated to 70-80 ml, and twice chromatographed on aluminum oxide. We obtained 3.8 g of base which was twice recrystallized from alcohol. Yield 2.45 g (9.5%). Glittering golden scales with m.p. 119-120°.

Found %: N 5.22, 5.45; S 24.78, 24.69. $C_{14}H_{11}NS_2$. Calculated %: N 5.45; S 24.90.

Ethyl p-toluenesulfonate of 2-methyl-6-styrylbenzthiazole. 2.51 g of 2-methyl-6-styrylbenzthiazole and 4 g of ethyl p-toluene sulfonate were heated on an oil bath for 12 hours at 150-160°. The salt was dissolved in boiling water, the water solution was washed with benzene, decolorized with animal charcoal, evaporated on the water bath, and heated to 120-125°. Yield 4.3 g (94%). For the synthesis of dyes the salt was used without further purification.

Ethyl p-toluene sulfonate of 2-methyl-6-(p-methoxystyryl)-benzthiazole. 0.56 g of 2-methyl-6-(p-methoxystyryl)-benzthiazole and 0.6 g of ethyl p-toluenesulfonate were heated 10 hours at 150-160°. The yield of salt was quantitative.

Ethyl p-toluenesulfonate of 2-methyl-6-(α-thienylvinyl)-benzthiazole. 1 g of 2-methyl-6-(α-thienylvinyl)-benzthiazole and 1.2 g of ethyl-p-toluenesulfonate were heated 10 hours at 140-150°. Yield 1.7 g (96%).

## Dyes

3,3'-Diethyl-6,6'-distyrylthiacarbocyanine iodide (I). A mixture of 1.3 g of ethyl p-toluenesulfonate of 2-methyl-6-styrylbenzthiazole, 1.3 g of orthoformic ester, and 8 ml of pyridine was boiled 30 min and poured into a hot aqueous solution of potassium iodide. The dye was filtered, washed with warm water, dissolved in 50 ml of pyridine, filtered, and to the hot solution was added 75 ml of boiling alcohol. The crystals which precipitated were separated and washed with alcohol and ether. Yield 0.34 g (34%). The bronze crystals melted 234-235°.

Found %: I 18.03, 18.06. $C_{37}H_{33}N_2S_2I$. Calculated %: I 18.24.

3,3'-Diethyl-9-methyl-6,6'-distyrylthiacarbocyanine bromide (II). 0.45 g of ethyl p-toluenesulfonate of 2-methyl-6-styrylbenzthiazole, 0.5 g of orthoacetic ester, and 3 ml of pyridine were boiled 35 min. The dye was precipitated by potassium bromide and crystallized from alcohol. Yield 0.1 g (30%). The crystals had a steely color; m.p. 272°.

Found %: Br 11.96, 11.62. $C_{38}H_{35}N_2S_2Br$. Calculated %: Br 12.06.

3,3',9-Triethyl-6,6'-distyrylthiacarbocyanine bromide. (III). A mixture of 0.45 g of ethyl p-toluenesulfonate of 2-methyl-6-styrylbenzthiazole, 0.5 g of orthopropionic ester, and 2 ml of pyridine was boiled 20 min. The dye was precipitated by potassium bromide. The thick, non-crystalline mass was washed with water and allowed to stand until the next day. The precipitate of the dye was filtered and twice crystallized from alcohol. Yield 0.16 g (48%). Glittering dark-green tablets; m.p. 199-200°.

Found %: Br 11.52, 11.50. $C_{39}H_{37}N_2S_2Br$. Calculated %: Br 11.81.

3,3'-Diethyl-6,6'-di-(p-methoxystyryl)-thiacarbocyanine bromide (IV). To a solution of 0.96 g of ethyl p-toluenesulfonate of 2-methyl-6-(p-methoxystyryl)-benzthiazole in 5 ml of pyridine was added 1 g of orthoformic ester and 5 drops of acetic anhydride; the mixture was boiled 30 min. The dye was precipitated by ether, dissolved in alcohol and converted to the bromide by the action of an alcoholic solution of potassium bromide. The bromide of the dye was filtered, washed with hot water, alcohol, and ether. Yield 0.48 g (71%). Dark-green crystals; m.p. 217°.

Found %: Br 11.12, 10.95; S 9.12, 9.30. $C_{39}H_{37}O_2N_2S_2Br$. Calculated %: Br 11.28; S 9.03.

3,3',9-Triethyl-6,6'-di-(p-methoxystyryl)-thiacarbocyanine iodide (V). A mixture of 0.96 g of ethyl p-toluenesulfonate of 2-methyl-6-(p-methoxystyryl)-benzthiazole, 1 g of orthopropionic ester, and 3 ml of pyridine was boiled for 35 min. The dye was precipitated by potassium bromide. After crystallization from alcohol the fine crystals weighed 0.24 g, and for further purification were dissolved in 50 ml of alcohol and precipitated by aqueous alcoholic solution of potassium iodide. After recrystallization from alcohol the crystals weighed 0.11 g (14%). Fine violet-black crystals; m.p. 243-244°.

Found %: I 15.87, 15.22. $C_{41}H_{41}O_2N_2S_2I$. Calculated %: I 16.20.

3,3'-Diethyl-6,6'-di-(α-thienylvinyl)-thiacarbocyanine bromide (VI). To a solution of 0.92 g of ethyl p-toluenesulfonate of 2-methyl-6-(α-thienylvinyl)-benzthiazole in 4 ml of pyridine was added 1 g of orthoformic ester and 5 drops of acetic anhydride. The mixture was boiled 20 min. The dye was precipitated by potassium bromide, crystallized from alcohol and then from glacial acetic acid. Yield 0.27 g (41%). Green crystals; m.p. 215°.

Found %: Br 12.07, 12.13. $C_{33}H_{29}N_2S_4Br$. Calculated %: Br 12.10.

3,3',9-Triethyl-6,6'-di-(α-thienylvinyl)-thiacarbocyanine bromide (VII). This was obtained in an analogous way from 0.92 g of ethyl p-toluenesulfonate of 2-methyl-6-(α-thienylvinyl)-benzthiazole and 1 g of orthopropionic ester. The dye was twice recrystallized from alcohol. Yield 0.25 g (36%). Green crystals; m.p. 199°.

Found %: Br 10.97, 11.08. $C_{35}H_{33}N_2S_4Br$. Calculated %: Br 11.61.

[3-Ethyl-4,5-benzobenzthiazole-2)] - [3-ethyl-6-styrylbenzthiazole-(2)]-trimethinecyanine iodide. (VIII). 0.45 g of ethyl p-toluene sulfonate of 2-methyl-6-styrylbenzthiazole and 0.54 g of ethyl p-toluenesulfonate of 2-β-acetanilidovinyl-4,5-benzobenzthiazole were dissolved in 5 ml of pyridine. To the solution was added 1 ml of acetic anhydride and the mixture was boiled for 20 min. The dye was precipitated by potassium iodide and crystallized from a mixture of 60 ml of alcohol and 10 ml of pyridine. Yield 0.2 g (31%). Green crystals; m.p. 208° (with decomposition).

Found %: I 19.77, 19.67. $C_{33}H_{29}N_2S_2I$. Calculated %: I 19.72.

[3-Ethyl-4,5-benzobenzthiazole-(2)] - [3-ethyl-6-(p-methoxystyryl)-benzthiazole-(2)]-trimethinecyanine iodide (IX). To a solution of 0.48 g of ethyl p-toluenesulfonate of 2-β-acetanilidovinyl-4,5-benzobenzthiazole in 10 ml of pyridine was added 0.54 g of ethyl p-toluenesulfonate of 2-methyl-6-(p-methoxystyryl)-benzthiazole and 1 ml of acetic anhydride. The mixture was boiled for 20 min. The dye was precipitated with potassium bromide, dissolved in chloroform, and chromatographed on aluminum oxide. The column was washed with ether. The dye was removed by methanol from the upper zone (dark blue) and was then precipitated by potassium bromide, dissolved in 40 ml of 50% acetic acid. The dark-green crystals melted at 181-183° (with decomposition).

Found %: I 18.75, 19.04. $C_{34}H_{31}ON_2S_2I$. Calculated %: I 18.84.

[3-Ethyl-4,5-benzobenzthiazole-(2)] - [3-ethyl-6-(α-thienylvinyl benzthiazole-(2)]-trimethinecyanine iodide (X). This was obtained in an analogous way from 0.48 g of ethyl p-toluenesulfonate of 2-β-acetanilidovinyl-4,5-benzobenzthiazole and 0.51 g of ethyl p-toluenesulfonate of 2-methyl-6-( α-thienylvinyl)-benzthiazole. The dye was purified as described above and was crystallized from nitromethane. Yield 0.1 g (17%). Violet black crystals; m.p. 196°.

Found %: I 19.74, 19.69. $C_{31}H_{27}N_2S_3I$. Calculated %: I 19.54.

[3-Ethyl-5-methoxybenzthiazole-(2)] - [3-ethyl-6-styrylbenzthiazole-(2)]-trimethinecyanine iodide (XI). A mixture of 0.45 g of ethyl p-toluenesulfonate of 2-methyl-6-styrylbenzthiazole, 0.52 g of ethyl 1 p-toluenesulfonate of 2-β-acetanilidovinyl-5-methoxybenzthiazole, 4 ml of pyridine, and 1 ml of acetic anhydride was boiled for 30 min. The dye was precipitated by potassium bromide, dissolved in alcohol, and transformed into the iodide. After it was crystallized from alcohol, the yield was 0.24 g (38%); m.p. 252°.

Found %: I 19.82, 19.77. $C_{30}H_{29}ON_2S_2I$. Calculated %: I 20.35.

[3-Ethyl-5-methoxybenzthiazole-(2)] - [3-ethyl-6-(p-methoxystyryl)-benzthiazole-(2)]-trimethinecyanine iodide (XII). This was obtained in an analogous way from 0.48 g of ethyl p-toluene sulfonate of 2-methyl-6-(p-methoxystyryl) benzthiazole and 0.52 g of ethyl p-toluenesulfonate of 2-β-acetanilidovinyl-5-methoxybenzthiazole. Yield 0.27 g (41%). Fine green crystals; m.p. 259°.

Found %: I 18.40, 18.30. $C_{31}H_{31}O_2N_2S_2I$. Calculated %: I 19.42.

3,3'-Diethyl-6'-styryl-4-keto-5-(3"-ethyl-6",7"-tetramethylenebenzthiazolinyliden -2"-α-phenylethylidene)-thiazolinothiacyanine p-toluenesulfonate (XIII). 0.95 g of 3-ethyl-5-(3'-ethyl-6',7'-tetramethylenebenzthiazolinyliden-2'-α-phenylethylidene)-thiazoliden-2-thione-4-one* and 1 g of dimethyl sulfate were heated on an oil bath for 25 min at 120°. After cooling, the quaternary salt was dissolved in 8 ml of pyridine and 0.9 g of ethyl p-toluenesulfonate of 2-methyl-6-styrylbenzthiazole was added and the mixture was heated 1 hour and 15 min at 120°. The precipitated rhodacyanine was filtered, and washed with methanol and ether. Yield 1.35 g (75%). Glittering green crystals; m.p. 303° (with decomposition).

Found %: S 15.07, 14.98. $C_{51}H_{49}O_4N_3S_4$. Calculated %: S 15.43.

0.5 g of the rhodacyanine (XIII) was dissolved in 230 ml of alcohol, the solution was filtered, the rhodacyanine was precipitated by potassium bromide and washed with hot water, methanol, and ether. Yield 0.3 g (68%). Glittering green tablets; m.p. 287° (with decomposition).

Found %: Br 9.98, 9.89. $C_{44}H_{42}ON_3S_3Br$. Calculated %: Br 9.95.

3,3'-Diethyl-6'-(p-methoxystyryl)-4-keto-5-(3"-ethyl-6",7"-tetramethylenebenzthiazolinyliden-2"-α-phenylethyliden)-thiazolinothiacyanine iodide (XIV). 0.6 g of merocyanine and 1 g of dimethyl sulfate were heated 25 min at 115-120°. To the pyridine solution of the quaternary salt of merocyanine was added 0.6 g of ethyl p-toluenesulfonate of 2-methyl-6-(p-methoxystyryl)-benzthiazole. The mixture was heated 1 hour 15 min at 120-125°. The rhodacyanine was precipitated by ether, dissolved in chloroform, and chromatographed on aluminum oxide. (It was necessary to protect the chromatographic column from the action of direct sunlight.) The column was washed with chloroform and acetone, and the rhodacyanine was eluted with methanol. The methanol was partly distilled off and the filtered solution was treated with an aqueous alcoholic solution of potassium iodide. The dye was washed with water, alcohol, and ether. Yield 0.43 g (39%). Green crystals with a bronze glint; m.p. 284°.

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*For the sake of brevity, this preparation will hereafter be called "merocyanine".

Found %: I 13.87, 13.98. $C_{45}H_{44}O_2N_3S_3I$. Calculated %: I 14.41.

3,3'-Diethyl-6'-(2-thienylvinyl)-4-keto-5-(3"-ethyl-6",7"-tetramethylenebenzthiazolinyliden-2"-α-phenylethyliden)-thiazolinothiacyanine iodide (XV). 0.95 g of merocyanine and 1 g of dimethyl sulfate were heated 20 min at 120-125°. After cooling, the quaternary salt was dissolved in pyridine, and to the solution was added 0.92 g of ethyl p-toluenesulfonate of 2-methyl-6-(2'-thienylvinyl)-benzthiazole. The mixture was heated 1 hour and 15 min at 120-125°, the rhodacyanine was precipitated by 30 ml of methanol, washed with ether, and purified as described above. The dye was precipitated by potassium iodide, and washed with water, methanol, and ether. Yield 0.41 g (24%). Green crystals; m.p. 294°.

Found %: I 14.78, 14.80. $C_{42}H_{40}ON_3S_4I$. Calculated %: I 14.82.

## SUMMARY

1. We obtained three new bases by the action of diazotized 2-methyl-6-aminobenzthiazole on acrylic acids: 2-methyl-6-styrylbenzthiazole, 2-methyl-6-(p-methoxystyryl)-benzthiazole, and 2-methyl-6-(α-thienylvinyl)-benzthiazole.

2. From these bases and ethyl p-toluenesulfonate, we synthesized the quaternary salts which contain unsaturated substituents in the 6-position of benzthiazole.

3. By condensation of the quaternary salts with ortho esters and intermediary compounds we obtained 7 symmetrical thiacarbocyanines, 5 unsymmetrical thiacarbocyanines, and 3 rhodacyanines, which contained unsaturated groups in the benzthiazole nucleus.

4. We showed that the introduction of unsaturated substituents in position 6 of the cyanine dye molecules shifted the absorption maxima sharply in the long wave portion of the spectra.

## LITERATURE CITED

[1] H. Meerwein, E. Buchner, and K. van Emster, J. pr. Ch. 152, 237 (1939).

[2] E. Muller, Angew. Chem. 61, 179 (1949); Ch. A. 44, 1428 (1950).

[3] W. Brunner and J. Kustatscher, Monatsh. 82, 100, (1951); W. Dale and C. Ise, J. Am. Chem. Soc. 76, 2259 (1954); W. Freund, J. Chem. Soc. 1952, 3068; 1953, 2889; F. Bergmann, E. Dimant, and H. Iaphe, J. Am. Chem. Soc. 70, 1618 (1948).

[4] G. Kon, J. Chem. Soc. 1948, 225; D. Brown and G. Kon, J. Chem. Soc. 1948, 2149; P. L'Ecuver, and C. Olivier, Can. J. Research 27 B, 689 (1949); Ch. A. 44, 2497 (1950).

[5] F. Bergmann, and D. Shapiro, J. Org. Ch. 12, 57 (1947); F. Bergmann, J. Weizmann and D. Shapiro, J. Org. Ch. 9, 408 (1944); P. L'Ecuyer, C. Olivier, F. Turcotte, G. Gigurere, and P. Roberge, Can. J. Research 26 B, 70 (1948); Ch. A. 42, 4989 (1948); R. Fuson and H. Cooke, J. Am. Chem. Soc. 62, 1182 (1940); P. L'Ecuyer, C. Olivier, Can. J. Research 28 B, 648 (1950); Ch. A. 45, 6605 (1951); F. Bell and D. Waring, J. Chem. Soc. 1948, 1024.

[6] J. Rai and K. Mathur, J. Indian Chem. Soc. 24, 413 (1947); Ch. A. 42, 5881 (1948); R. Fusco and S. Rossi, Gazz. 78, 524 (1948); Ch. A. 43, 1744 (1949).

[7] S. Cristol and W. Norris, J. Am. Chem. Soc. 76, 3008 (1954).

[8] W. Brunner and H. Perger, Monatsh. 79, 187 (1948); Ch. A. 44, 1054 (1950).

[9] C. Koelsch and V. Boekelheide, J. Am. Chem. Soc. 66, 412 (1944); C. Koelsch, J. Am. Chem. Soc. 65, 57 (1943).

[10] E. Coyner and G. Ropp, J. Am. Chem. Soc. 70, 2283 (1948); E. Braude and J. Fawcett, J. Chem. Soc. 1951, 3113.

[11] H. Mahra and K. Mathur, J. Indian Chem. Soc. 33, 618 (1956).

[12] U. Waters, Chemistry of Free Radicals, IL, 176 (1948).*

[13] I. Kochi, J. Am. Chem. Soc. 77, 5090, 5274 (1955); 78, 1228 (1956).

[14] W. King and F. Nord, J. Org. Ch. 13, 635 (1948); Synthesis of Organic Preparations, 4, 475 (1953).

[15] V. M. Zubarovskii, DAN SSSR 83, 85 (1952).

[16] W. King and F. Nord, J. Org. Ch. 14, 409 (1949).

[17] R. Robinson and J. Shinoda, J. Chem. Soc. 127, 1977 (1925).

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# MONOANILS OF GLUTACONIC ALDEHYDE

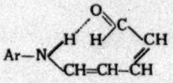
## I. DERIVATIVES OF PRIMARY AROMATIC AMINES

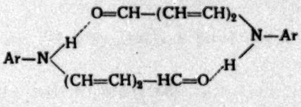
N. E. Grigor'eva and A. A. Pechka

By treatment of pyridine 2,4-dinitrochloroarylates with alkali, Zincke [1] obtained red compounds which readily formed hydrazones and condensed with primary aromatic amines. He considered it probable that they had a structure with an open pentamethine chain formed as a result of fission of the pyridine ring. He ascribed a similar structure to the compounds obtained by treatment of N-substituted pyridine dyes with alkali [2]. These compounds are known under the name of "Zincke aldehydes"; they are described also in the works of other authors [3]. Of the primary-amine derivatives, only dinitro-substituted ones were known [1]. The corresponding derivatives of aniline [4] and other primary aromatic amines [5] were prepared by one of us. However, the nature of these compounds was not investigated in detail, since they were obtained in low yields. For the purpose of making a more thorough study of similar compounds we developed a method of preparation of derivatives of aniline and other amines, achieving considerable yields in some cases, and determined their capacity for condensation with aromatic amines and with compounds containing active methyl groups.

By analogy with known Zincke aldehydes we considered the compounds which we obtained to be monoanils of glutaconic aldehyde; however, unlike Zincke aldehydes, they do not condense with primary aromatic amines under similar conditions, and they form hydrazones with difficulty. We carried out the condensation of the monoanils with aromatic amines under varied conditions: in acetic acid in the presence of hydrochloric acid, in acetic anhydride in the presence of hydrogen chloride, and in pyridine in the presence of hydrogen chloride. In the last case only, a color change was observed, which could be used as an indication of reactions taking place. On reaction of the unsubstituted monoanil with aniline hydrochloride in pyridine a pronounced deepening of color occurred; a red, crystalline substance was obtained, which proved to be the monoanil hydrochloride. A similar substance was obtained on reaction of p-anisidine hydrochloride with the unsubstituted monoanil. Monoanils which were derivatives of other amines exhibited similar behavior, but their hydrochlorides were very hygroscopic and were not isolated. Therefore, in the reaction of monoanils with amine hydrochlorides in pyridine, transfer of hydrogen chloride from the amine to the monoanil is all that occurs; we were not able to obtain the expected mixed pentamethine dye in a single case [6]. Secondary aromatic amines did not react with the monoanils under investigation, either.

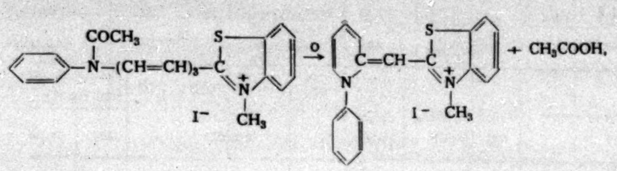
The negative results of the attempts at condensation of glutaconic aldehyde monoanils with aromatic amines is difficult to explain if it is assumed that they contain a free carbonyl group. Furthermore, glutaconic aldehyde monoanils, like other carbonyl compounds [7], deepen in color in the presence of acids. Spectroscopic investigations of glutaconic aldehyde monoanils showed that they are amphoteric compounds; the dual reactivity and the possibility of formation of a hydrogen bond (which may be either intra- or intermolecular) apparently cause inertness of the carbonyl group in these compounds in certain reactions. Dinitro-substituted



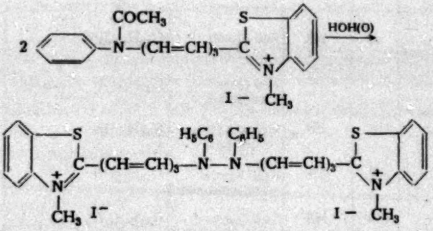


monoanils apparently have little tendency toward similar conversions, owing to the ortho-effect between the nitro and amino groups.

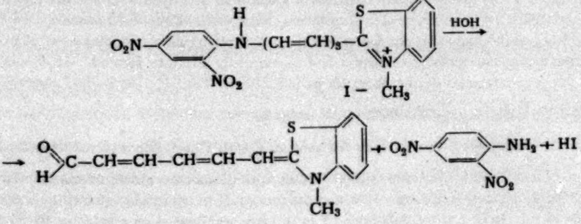
The capacity of the monoanils obtained by us for condensation with compounds containing active methyl groups may serve as an indirect proof of their structure. We carried out the condensation of the unsubstituted monoanil, and also the p-methyl-p-methoxy- and 2,4-dinitromonoanils, of glutaconic aldehyde with 2,3-dimethylbenzothiazolium iodide under varying conditions. The first three monoanils formed red-violet dyes as end-products; in the case of the aniline derivative an intermediate blue dye was obtained. The violet dyes and the intermediate blue dye react differently to acid; the violet dyes are decolorized on addition of excess acid, whereas the color of the blue dye is not visibly changed. The heightening of the color on heating suggests the hypothesis that a mixed hexamethine dye (hemicyanine) is formed at first and is then acetylated on heating; however, analytical data do not confirm this hypothesis. The low yields of the dyes and their color suggest that the hexamethine dye initially formed undergoes oxidative condensation with the formation either of an unsummetrical pyridocyanine,



or of a bisazomethine dye



On condensation of the 2,4-dinitromonoanil with 2,3-dimethylbenzothiazolium iodide a yellow-brown substance was obtained, which contained neither the dinitrophenyl radical nor halogen. It is possible that the hexamethine dye first formed decomposes according to the scheme



Although the nature of the products of condensation of glutaconic aldehyde monoanils with 2,3-dimethylbenzothiazolium iodide has not been finally established (further investigation is required), the experiments which have been done show that under corresponding conditions glutaconic aldehyde monoanils are capable of reactions characteristic of carbonyl compounds.

## EXPERIMENTAL

In order to increase the yields of glutaconic aldehyde monoanils we made certain changes in the method developed earlier [8]. After addition of a 15% excess of sodium hydroxide solution to a concentrated arylpyridinium chloride solution (until yellow material ceased to appear at the point where a drop of the alkali solution fell), the mixture was heated in a water bath at 60-70° until the initially formed resin crystallized and the pseudobase was entirely converted to the monoanil (5-10 minutes). The characteristics of the glutaconic aldehyde monoanils investigated by us are given in Table 1.

TABLE 1

Glutaconic Aldehyde Monoanils

| Name of compound | Yield (%) | Melting point | Color of crystals | Empirical formula | Nitrogen content (in %) calc. | Nitrogen content (in %) found |
|---|---|---|---|---|---|---|
| 1-(Phenylamino)-pentadien-1,3-al-5 [4] | 74 | 171° | Red-violet | $C_{11}H_{11}ON$ | 8.09 | 8.12 |
| 1-(p-Methylphenylamino)-pentadien -1,3-al-5[4] | 79 | 176 | Brown-red(from benzene | $C_{12}H_{13}ON$ | 8.00 | 8.05 |
| 1-(p-Methoxyphenylamino)-pentadien-1,3-al-5 | 60 | 165 | Red (from acetone) | $C_{12}H_{13}O_2N$ | 7.30 | 7.38 |
| 1-(p-Biphenylamino)-pentadien-1,3-al-5 | | | Red (from acetone) | $C_{17}H_{15}ON \cdot {}^1/_2C_2H_6O$ | 5.03 | 5.16 |
| 1-(α-Naphthylamino)-pentadien-1,3-al-5 | 65 | 207 | Orange (from benzene) | $C_{15}H_{13}ON$ | 6.28 | 6.44 |
| 1-(β-Naphthylamino)-pentadien-1,3-al-5 | 65 | 201 | Red-brown from benzene) | $C_{15}H_{13}ON$ | 6.28 | 6.35 |
| 1-(2,4-Dinitrophenylamino)-pentadien-1,3-al-5 [1] | 90 | 159 | Red (from dichloroethane) | $C_{11}H_9O_5N_3$ | 15.97 | 15.86 |

The condensations of the unsubstituted monoanils of glutaconic aldehyde with aniline and p-anisidine hydrochlorides were carried out with equimolar proportions in the cold. Thus, for instance, to a thoroughly ground mixture of 0.6 g of the monoanil and 0.4 g of aniline hydrochloride was added 5 ml of pyridine. In this case the solution turned red-violet, and after a few minutes a precipitate formed. After washing with ether and drying, the precipitate weighed 0.38 g. M. p. 112°.

Found %: N 6.70, 6.62. $C_{11}H_{11}ON \cdot HCl$. Calculated %: N 6.68.

On treatment of an aqueous solution of the red substance with alkali, the original monoanil was obtained.

Condensation of 2,3-dimethylbenzothiazolium iodide with glutaconic aldehyde monoanils. The condensation of 2,3-dimethylbenzothiazolium iodide and the monoanil in equimolar quantities was carried out in acetic anhydride (5 ml for 1 g of the mixture). The mixture was heated on a grid for 40-50 minutes (until a stable, unchanging color appeared) and left for 12 hours. The crystals which had separated out were then washed in the filter with ether and water and were recrystallized (Table 2).

TABLE 2

Products of Condensation of 2,3-Dimethylbenzothiazolium Iodide with Glutaconic Aldehyde Monoanils

| Amine, the derivative of which is the monoanil brought into condensation | Duration of the condensation (in min) | Melting point | Color of crystals (solvent) | Absorption maximum ($\lambda_{max}$) in ethanol (in mμ) | Assumed empirical formula | Nitrogen content (in %) | |
|---|---|---|---|---|---|---|---|
| | | | | | | calc. | found |
| Aniline . . . . | 40 | 339° | Violet (from alcohol) | 565 | $C_{20}H_{17}N_2SI$ | 6.31 | 6.49 |
| Aniline . . . . | 8 | — | Golden-green from alcohol) | 648[*] | $C_{22}H_{21}ON_2SI$<br>$C_{23}H_{21}N_2S_2I$ | 5.76<br>5.43 | 5.47 |
| p-Toluidine . . | 40 | 240 | Green (from dichloroethane) | 562 | $C_{21}H_{18}N_2SI \cdot C_2H_4Cl_2$ | 5.03 | 4.87 |
| p-Anisidine . . | 40 | — | Violet (from alcohol | 560 | $C_{21}H_{21}ON_2SI$ | 5.88 | 5.96 |
| 2,4-Dinitroaniline | 50 | 259 | Brown (from glacial acetic acid) | — | $C_{14}H_{13}ONS$ | 5.76 | 5.70 |

## SUMMARY

1. Glutaconic aldehyde monoanils which are derivatives of primary aromatic amines have been investigated.

2. It has been shown that neither the unsubstituted monoanil of glutaconic aldehydes nor those which contain electron-donor substituents in the aromatic rings condense with aromatic amines.

3. The condensation of several monoanils with 2,3-dimethylbenzothiazolium iodide has been carried out; condensation products were obtained, the structure of which has not been definitely established. Hypotheses on the structure of the products obtained are stated.

## LITERATURE CITED

[1] Th. Zincke, Heuser and Moller, Lieb. Ann. 33, 296 (1904); Th. Zincke, Lieb. Ann. 408, 285 (1914).

[2] Th. Zincke, Lieb. Ann. 338, 107 (1905); 353, 380 (1907).

[3] W. Konig, J. pr. Ch. 85, 353 (1912).

[4] N. E. Grigor'eva and M. D. Iavlinskii, Ukr. Chem. J. 18, 82 (1952).

[5] N. E. Grigor'eva and L. K. Gintse, J. Gen. Chem. 24, 169 (1954);[**] 26, 232 (1956).[**]

[6] Th. Zincke, Lieb. Ann. 338, 133 (1905).

[7] P. Pfeifer, Organische Molekularverbindungen, Stuttgart (1927).

[8] N. E. Grigor'eva, A. B. Organes'ina, and L. A. Mysh, J. Gen. Chem. 27, 1565 (1957).[**]

[9] L. Hofer, R. Grabenstettev, and E. Wiig, J. Am. Chem. Soc. 72, 203 (1950).

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[*] For the coresponding non-acylated hexamethine dye, the absorption maximum in ethyl alcohol is given a 613 mμ [9].

[**] Original Russian pagination. See. C.B. Translation.

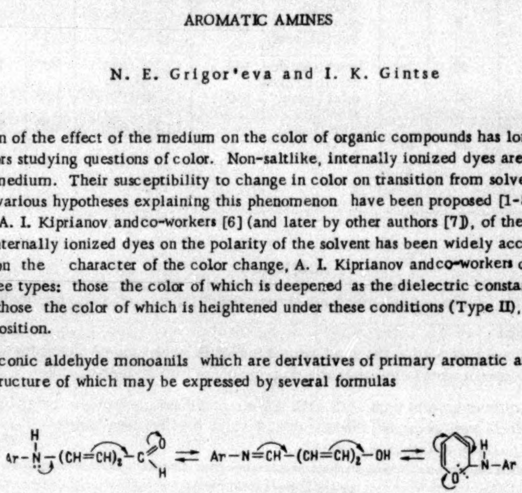
# MONOANILS OF GLUTACONIC ALDEHYDE

## II. EFFECT OF THE MEDIUM ON THE COLOR OF DERIVATIVES OF PRIMARY AROMATIC AMINES

N. E. Grigor'eva and I. K. Gintse

The question of the effect of the medium on the color of organic compounds has long received the attention of investigators studying questions of color. Non-saltlike, internally ionized dyes are especially sensitive to change in the medium. Their susceptibility to change in color on transition from solvent to solvent has long been known, and various hypotheses explaining this phenomenon have been proposed [1-5]. The hypothesis, first advanced by A. I. Kiprianov and co-workers [6] (and later by other authors [7]), of the dependence of the color change in internally ionized dyes on the polarity of the solvent has been widely accepted by organic chemists. Depending on the character of the color change, A. I. Kiprianov and co-workers divide internally ionized dyes into three types: those the color of which is deepened as the dielectric constant of the solvent decreases (Type I), those the color of which is heightened under these conditions (Type II), and those which occupy an intermediate position.

Those glutaconic aldehyde monoanils which are derivatives of primary aromatic amines are tautomeric compounds, the structure of which may be expressed by several formulas

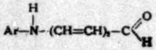


These compounds belong to the class of internally ionized compounds, and each of the given forms may be represented as a dipolar ion. Compounds of this type are very sensitive to a change of medium – they change color in various "neutral" solvents in the presence of acids or alkalis.

Unlike the internally ionized compounds investigated earlier [6, 7], no definite dependence between the color change and the polarity of the solvent is observed in the case of glutaconic aldehyde monoanils. The peculiarities in the structure of these compounds and the variations of their color in different media were grounds for a more thorough investigation of them for the purpose of elucidating the factors which affect the change of absorption of internally-ionized compounds. The relatively good solubility of the monoanils permitted investigation of their absorption spectra in many organic solvents; the spectra of the unsubstituted monoanils in solvent mixtures were also investigated. The absorption spectra of seven monoanils derived from primary amines and, for comparison, a methylaniline derivative were determined in neutral, acid, and alkaline media.

Discussion of absorption spectra. On comparison of the absorption maxima of glutaconic monoanils (Table 1) in a single solvent, e.g., butyl alcohol, it is evident that the character of the aromatic radical has a considerable effect on the variation in color of the monoanils. As the basicity of the amino radical decreases, the color of the monoanil is heightened; the 2,4-dinitroaniline derivative (VII) is the most "highly" colored. Unlike the absorption spectra of other derivatives of primary aromatic amines, that of the 2,4-dinitromonoanil varies little from solvent to solvent; the tendency toward displacement of the absorption maximum toward the long-wave part of the spectrum is noticeable only in strongly polar solvents. Comparison of the data of

TABLE 1

Absorption Maxima (in mμ) of Glutaconic Aldehyde Monoanils of the Type  $Ar-N(H)-(CH=CH)_n-C(=O)H$ in Various Solvents (values of $\epsilon \cdot 10^{-4}$ are given in parentheses)

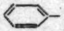
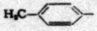
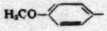
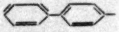
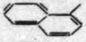
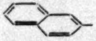
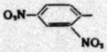
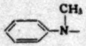
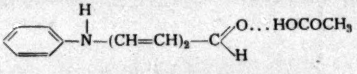
| No. of compound | Ar | Alcohol | | | Acetone | Pyridine | Dichloro-ethane | Acetic acid | Dioxane | Benzene | Bromo-benzene | Nitro-benzene |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | methyl | ethyl | n-butyl | | | | | | | | |
| (I) |  | 440 (1.8) | 442 (1.9) | 445 (1.8) | 471 (2.5) | 480 (2.3) | 462 (1.74) | 495 (2.9) | 508 (1.5) | 485 (1.9) | 480 | 515 (0.68) |
| (II) |  | 442 (1.5) | 446 (1.8) | 452 (1.6) | 475 (2.5) | 482 (2.1) | 461 (1.2) | 500 (2.6) | Red | 486 (1.6) | — | 523 (1.8) |
| (III) |  | — | 450 (1.8) | 452 (1.5) | 474 (1.9) | 482 (1.8) | 462 | 492 (1.3) | — | 486 (1.4) | — | 532 |
| (IV) |  | — | — | 450 (0.7) | — | 495 (1.2) | — | 509 (1.5) | 472 | 495 (1.2) | — | — |
| (V) |  | 430 (2.1) | 435 (2.0) | 446 (1.8) | 471 (2.6) | 481 (2.5) | 460 (1.2) | 494 (1.3) | — | 483 (1.9) | — | 505; 470 (1.3) |
| (VI) |  | 450 (0.5) | 455 (1.9) | 462 (1.8) | 483 (1.4) | 500 (1.9) | 475 (1.3) | 509 (3.0) | Red | 497 (2.0) | — | 530; 520 (0.76) |
| (VII) |  | — | 397 (3.2) | 387 (2.2) | — | — | 387 (3.0) | 387 (3.0) | — | — | — | 442 (1.8) |
| (VIII) |  | — | 380 (6.3) | 380 (4.3) | 367 (5.4) | 380 (4.0) | 350 (3.0) | 390 (3.4) | — | 367 (3.8) | — | — |

Table 1 shows that in alcohols the displacement of the absorption maximum for compounds (I) – (VIII) is slight, although the polarity of the alcohols varies. The color is noticeably deeper in acetone (displacement of maximum, 20-26 mμ toward the long-wave end), whereas the polarity of the latter is only slightly greater than that of butyl alcohol. If the color change of monoanil (I) is followed thru 11 solvents, no definite dependence between the color change and the polarity of the solvent can be established; the color change varies, depending on the choice of solvent. For instance, in a series of solvents: alcohols, dichloroethane, bromobenzene, benzene, and dioxane the color is deepened as the dielectric constant of the solvent decreases (Type I). In such solvents as nitrobenzene, acetone, and dichloroethane the color is heightened as the polarity of the solvent decreases (Type II). In the series methyl alcohol – dichloroethane (excepting acetone) this compound may be referred to the intermediate type, as regards color change. Apparently no dependence can be established between the variation in the dipole moment of the solvent and the color of the monoanil; thus the color of a benzene solution of monoanil (I) differs little from that of a pyridine solution, although the dipole moments of these solvents are quite different.

The variation in the absorption of monoanil (I) in solvent mixtures is shown in Table 2. The monoanil was dissolved in a definite volume of one solvent, and the solution was then diluted with a second solvent; the spectra of the solutions were determined when the latter were freshly prepared and again, one day later. As is evident on comparison of the data given in Table 2, dilution of the alcoholic solution with acetone does not affect the light absorption; the latter is the same as in the alcoholic solution. Dilution of the acetone solution with alcohol markedly changes the absorption, and the latter approaches the absorption of the alcoholic solution. It is quite obvious that in the reaction of the monoanil with the alcohol a compound (complex) is formed, more stable than that formed in the reaction of the monoanil with acetone. The stability of the complexes is probably due to the difference in basicity between the alcohol and acetone. The variation in the absorption of solutions in alcohol – pyridine mixtures is even more pronounced. These solvents differ markedly in basicity; if the monoanil reacts with the alcohol as a base, then it acts as an acid in pyridine. In alcohol – benzene mixtures the absorption is only slightly dependent on the solvent ratio and the order of solution of the monoanil. It is scarcely probable that the monoanil would react with benzene; obviously, in benzene solution the light is absorbed by neutral monoanil molecules. The absorption of the monoanil in alcohol-benzene solution is due mainly to the monoanil-alcohol complex; this complex does not dissociate even when the alcoholic solution is greatly diluted (25 : 75). In pyridine–benzene mixtures, regardless of the solvent ratio, the absorption approximates that of a pyridine solution; after a day the absorption maximum coincides with the additive one.

The variation in the absorption of solutions of monoanil (I) in mixtures of two solvents clearly shows that this absorption is not connected with the polarity of the solvents (since, when the ratios are the same, the polarity is the same). The absorption depends on which of the solvents was the first wherein the monoanil was dissolved; i.e., it depends on the structure and stability of the monoanil–solvent complex.

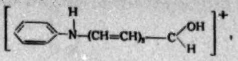
On comparison of the absorption curves of monoanil (I), shown in Figure 1, variations in the spectra, depending on the nature of the solvents, are clearly evident. The great difference between the spectra of the monoanil in butyl alcohol and in acetic acid is due not to the difference in polarity between these solvents, but mainly to the structure of the compounds formed by the monoanil with the solvents. Acetic acid is a weak acid, and mainly undissociated molecules react with the monoanil. The attachment of the acid to the carbonyl group oxygen causes halochromic deepening of the color [8].



$$C_6H_5-\overset{H}{N}-(CH=CH)_2-C\begin{matrix}\nearrow O\ldots HOCOCH_3\\ \searrow H\end{matrix}$$

The acid may be attached also to the amino group of the monoanil.

In this case "deactivation" of the auxochrome leads to heightening of the color, and the band with maximum at 375 mμ possibly belongs to the ammonium salt. After diluting the acetic acid solution with butyl alcohol a deepening of the color is observed. The intensity of the bands in the visible and near-ultraviolet regions decreases (the monoanil concentration being the same throughout), but the absorption in the farther ultraviolet becomes more pronounced. The increase in the polarity of the solution, observed after diluting with butyl alcohol, increases the degree of dissociation of the acetic acid [9] and facilitates the formation



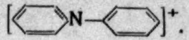
of the carbonium salt which causes the deepening of the color. The carbonium salt is not stable; a molecule of water is easily split off from it with formation of the corresponding pyridine salt: . This process takes place more rapidly when the alcoholic solution is diluted with acetic acid.

TABLE 2

Absorption Maxima (in mμ) of Glutaconic Aldehyde Monoanil (I) in Solvent Mixtures (values of $\epsilon \cdot 10^{-4}$ are given in parentheses)

| Solvent mixtures | Ratio (in vol. %) | Absorption in mixtures | | Additive absorption |
|---|---|---|---|---|
| | | immediately after mixing | 24 hours later [*] | |
| Alcohol–acetone | 75 : 25 | 442 (1.90) | — | 456.5 (2.05) |
| | 50 : 50 | 443 (1.88) | — | |
| | 25 : 75 | 443 (1.98) | — | |
| Acetone–alcohol | 25 : 75 | 443 (1.98) | — | |
| | 50 : 50 | 443 (1.83) | — | |
| | 75 : 25 | 455 (1.90) | 455 (1.80) | |
| Alcohol–pyridine | 75 : 25 | 445 (1.90) | 445 (1.80) | 461 (2.08) |
| | 50 : 50 | 450 (1.80) | 450 (1.88) | |
| | 25 : 75 | 452 (1.86) | 465 (1.90) | |
| Pyridine–alcohol | 25 : 75 | 445 (1.90) | 445 (1.90) | |
| | 50 : 50 | 471 (1.78) | 450 (1.90) | |
| | 75 : 25 | 473 (2.3 ) | 468 (1.93) | |
| Alcohol–benzene | 75 : 25 | 445 (1.88) | 445 (1.83) | 463.5 (1.83) |
| | 50 : 50 | 448 (1.95) | 448 (1.78) | |
| | 25 : 75 | 448 (1.67) | 458 (1.72) | |
| Benzene–alcohol | 25 : 75 | 445 (1.75) | 445 (1.95) | |
| | 50 : 50 | 448 (1.81) | 448 (1.90) | |
| | 75 : 25 | 465 (1.69) | 470 (1.74) | |
| Pyridine–benzene | 75 : 25 | 480 (2.16) | 482 (2.14) | 482.5 (2.00) |
| | 50 : 50 | 481 (2.16) | 482 (2.14) | |
| | 25 : 75 | 481 (2.05) | 483 (2.07) | |
| Benzene–pyridine | 25 :75 | 480 (2.05) | 482 (2.14) | |
| | 50 :50 | 481 (2.16) | 482 (2.14) | |
| | 75 :25 | 481 (2.05) | 483 (2.07) | |

Deepening of the color in the presence of acids is observed in the cases of monoanils (I)–(VI), the color changing considerably on transition from solvent to solvent (Table 1). For instance, the absorption maximum of monoanil (I) in the presence of hydrogen chloride is displaced toward the long-wave end in such solvents as acetone (501 mμ), butyl alcohol (510 mμ), dichloroethane (525 mμ), and benzene (536 mμ). In the presence of acid the less polarity the solvent has, the deeper and more stable the color is. In more polar solvents – methyl and ethyl alcohols – the solutions are instantly decolorized in the presence of hydrogen chloride. These facts confirm the above-stated explanation of the change in monoanil spectra in an acid medium.

The change in color of monoanils derived from primary amines takes place in time in the presence of alkali. The change in absorption of monoanil (I) is shown in Table 3.

The deepening of the color in the presence of alkali is due to tautomeric conversion; the sodium enolate is formed at a varying rate depending on the basicity of the monoanil, and the stabilities of the salts are unequal.

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[*] The spectra of monoanil (I) in the individual solvents were unchanged one day later.

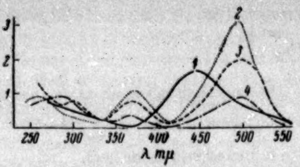


Fig. 1. Absorption spectra of monoanil (I). 1) In n-butyl alcohol; 2) in glacial acetic acid; 3) in acetic acid + 50% n-butyl alcohol; 4) in n-butyl alcohol + 50% acetic acid.

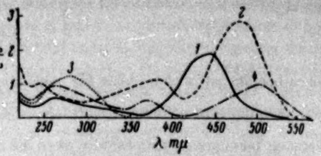


Fig. 2. Absorption spectra of monoanil (I). 1) In ethyl alcohol; 2) in ethyl alcohol + 250 equiv. NaOH; 3) in ethyl alcohol + 10 equiv. HCl; 4) in ethyl alcohol + 250 equiv. NaOH + 300 equiv. HCl.

Since the Na-enolate of the monoanil derived from aniline is unstable the equilibrium is gradually displaced toward the monoanil, which causes a heightening of the color. For complete conversion of the monoanil to the enolate a definite excess of alkali is necessary, after which further addition of alkali has no effect on the absorption; for the aniline derivative this excess is equal to 25 equiv. of NaOH. We noted above, that addition of acid to a solution of monoanil (I) in ethyl alcohol causes the color to vanish. If an excess of acid is quickly added to an alkaline solution of the monoanil in ethyl alcohol, the color is deepened; the intensity of the band increases if the acid is added within 20-30 minutes after alkalization of the solution (Table 3). The alkali decreases the polarity of the alcoholic solution, and the acid reacts with the Na-enolate of the monoanil, forming a deeply-colored salt which slowly dissociates under these conditions. When the alkali is gradually neutralized with acid, the solution is decolorized.

TABLE 3

Change in Absorption Maxima of Glutaconic Aldehyde Monoanil (I) in Dependence on the Time of Standing of the Solution (values of $\epsilon \cdot 10^{-4}$ are given in parentheses)

| Solvent | Ethyl alcohol | | Ethyl alcohol + NaOH | | | Ethyl alcohol + + NaOH + excess HCl | |
|---|---|---|---|---|---|---|---|
| Time (in min) | 0 | 20 | 0 | 0.5 | 20 | 0 | 0.5 |
| $\lambda_{max.}$ (in mμ) | 442 (1.9) | 442 (1.9) | 470 (1.9) | 480 (2.4) | 470 (2.3) | 502 (1.3) | 502 (2.0) |

Changes in the spectra of monoanil (I), due to changes in the medium, are evident on comparison of the curves shown in Figure 2. The analogy in the character of the spectra in acid and alkaline media indicates that in both cases analogous transformations in the structure of the monoanil molecule take place.

The character of the reaction of monoanils with acid and alkali is connected with the basicity of the monoanils. Thus, for instance, the 2,4-dinitromonoanil (VII) is not sensitive to acids; its absorption spectra in ethyl alcohol and in acetic acid nearly coincide. The color of this compound is markedly deepened in the presence of alkali, and it changes on transition from solvent to solvent (Figure 3). Although the absorption maxima of the 2,4-dinitromonoanil are displaced with respect to one another, the main bands lie in the same region; therefore the change of color is due to the varying stability of the anion in solvents of different polarity.

The peculiarities in the variation of the color of glutaconic aldehyde monoanils, derived from primary aromatic amines, in different solvents apparently could be explained by the presence of "mobile" hydrogen on the amino-group nitrogen, which increases the degree of reaction of the monoanil with the solvent. This hypothesis is partly confirmed; the change in the absorption of the N-methylmonoanil (VIII) [10] on transition from solvent to solvent is less than that for the unsubstituted monoanil (I) (Table 1), but it, also, is independent of the polarity of the solvent.

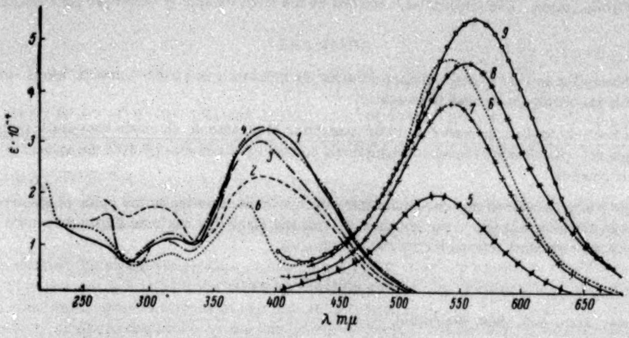


Fig. 3. Absorption spectra of monoanil (VII). 1) In ethyl alcohol; 2) in n-butyl alcohol; 3) in dichloroethane; 4) in acetic acid; 5) in methyl alcohol + NaOH; 6) in ethyl alcohol + NaOH; 7) in n-butyl alcohol + NaOH; 8) in dichloroethane + NaOH; 9) in acetone + NaOH.

Replacement of amino-group hydrogen by alkyl causes a pronounced hypsochromic shift of the absorption maximum; in benzene, for instance, the shift is equal to 118 mμ, which may be due to a decrease of conjugation in the molecule. However, a formula with an open pentamethine chain terminated by groups of diverse character cannot explain either the cause of the pronounced heightening of color or that of other peculiarities in the behavior of the N-methylmonoanil. Unlike the case of the unsubstituted monoanil (I), alkali does not affect the displacement of the absorption maximum of the N-methylmonoanil (VIII), which confirms the tautomeric conversion of monoanil (I). In the presence of hydrogen chloride the color is not deepened in any of the solvent investigated, but the monoanil is decomposed; in the spectrum the band of glutaconic aldehyde in an acid medium [11] (Figure 4) appears. All these peculiarities in the absorption of the N-methylmonoanil are easily explained if it is assumed that the latter has a cyclic structure (VIIIa) [12].

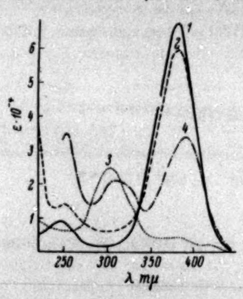
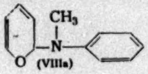


Fig. 4. Absorption spectra of monoanil (VIII). 1) In ethyl alcohol; 2) in ethyl alcohol + 250 equiv. HCl; 3) in ethyl alcohol + 250 equiv. HCl; 4) in acetic acid.



(VIIIa)

The facts, stated above, on the color change of glutaconic aldehyde monoanils confirm the hypothesis, advanced earlier, [4, 5], that the variation of color of nonsaltlike dyes in different solvents depends on the structure of the complexes formed by the dye with the solvent. They, in turn, are in accord with the investigations of N. A. Izmailov [13], who established that the variation of acid dissociation constants in different solvents is due to the formation of acid-solvent complexes.

The variation in the color of monoanils in different solvents in the presence of acids and alkali is convincing evidence of the fact that there is no difference in principle between solvatochromy and halochromy. In both cases an acid-base reaction takes place. The variation of the color in different solvents is due to displacement of the equilibrium: dye + solvent (acid, base) $\rightleftarrows$ complex (salt).

The absorption spectra were determined with an SF-4 spectrophotometer in the ultraviolet and with an SF-2M in the visible region. The solvents were purified by the methods usually employed for spectroscopy.

## SUMMARY

1. The absorption spectra of eight glutaconic aldehyde monoanils in various solvents, alone and in the presence of acids and alkali, have been investigated.

2. It has been shown that the variation in the absorption of glutaconic aldehyde monoanils in different solvents is connected with the structure of the complexes formed by the monoanil with the solvent if a reaction between them is possible.

3. Certain views have been expressed concerning the causes of variation of the color of glutaconic aldehyde monoanils in different solvents in the presence of acids and alkali. It has been shown that there is no difference in principle between solvatochromy and halochromy.

## LITERATURE CITED

[1] Schlenk, Lieb. Ann. 368, 294 (1909).

[2] Hantsch, Ber. 52, 525 (1919); Hantsch and Voigt, Ber. 62, 971 (1929).

[3] Burawoy, Ber. 63, 3155 (1930); 64, 462 (1931).

[4] Konig, J. pr. Ch. 112, 1 (1926).

[5] G. Scheibe, Ber. 58, 598 (1952); 59, 2617 (1926); 60, 1406 (1927).

[6] A. L. Kiprianov and V. E. Petrun'kin, J. Gen. Chem. 10, 600, 613 (1940); A. I. Kiprianov and E. S. Timoshenko, J. Gen. Chem. 17, 1468 (1947); Ukr. Chem. J. 18, 347 (1952).

[7] Brooker, Keyes, and Heselstine, J. Am. Chem. Soc. 73, 5350 (1951); Knott and Fischer, J. Chem. Soc., 1955, 3313.

[8] Pfeifer, Organische Molekularverbindungen, Stuttgart (1927).

[9] A. I. Shatenshtein, Theory of Acids and Bases, State Chem. Press (1949).*

[10] Th. Zincke, Lieb. Ann. 338, 107 (1905).

[11] N. E. Grigor'eva, I. K. Gintse and A. P. Severina, J. Gen. Chem. 26, 3096 (1956).**

[12] W. Konig, J. pr. Ch. 70. 19 (1904).

[13] N. A. Izmailov, J. Anal. Chem. 4, 267 (1947); J. Phys. Chem. 24, 321 (1950); 28, 2047 (1954).

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*In Russian.

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# INVESTIGATION OF ANODE DEPOSITS FORMED IN THE ELECTROLYSIS OF SOLUTIONS OF CERTAIN THALLIUM SALTS. III

M. S. Skanavi-Grigor'eva and V. I. Staroverova

The study of the properties of thallium and its compounds is now an important problem of chemical science. This element is finding ever-increasing practical application. Thallium is an accessory element in lead-zinc ores. In the present method of electrolytic separation of zinc at the cathode the possibility of formation of thallium oxides at the anode, in the form of anode deposits, should be taken into account; such deposition of thallium oxides on the anode may take place in the electrolytic preparation of thallium.

The possibility of obtaining anode deposits from solutions of thallium salts (nitrate and sulfate) has repeatedly been pointed out by various authors. However, neither the conditions for obtaining anode deposits nor the composition of the latter was definitely established in earlier works. It was assumed that anode deposits consists of higher oxides of thallium, but the oxidation states were not precisely specified. Some authors consider the deposits to be composed of oxides of tervalent thallium [1-7]; others consider them to consist of a mixture of the oxides of 3- and 4-valent thallium [4, 5] or a peroxide of thallium [8], similar to the peroxides of potassium, rubidium, and other metals. The addition of various organic substances such as alcohol, oxalic or benzoic acid, acetone, etc., was considered a necessary condition for carrying out electrolysis.

The purpose of the present work is to answer the following questions: 1) under what conditions of electrolysis of thallium-salt solution the anode deposits are best formed; 2) what the composition of these deposits is; i.e., whether they are oxides of thallium in one valence state or another or have a more complicated composition; 3) whether complex formation affects the composition of the deposit or the conditions of its production.

## EXPERIMENTAL

For investigation of the anode deposits obtained on electrolysis of thallium-salt solutions we chose the following soluble thallous salts: the nitrate, fluoride, sulfate, and carbonate and the complex salts of silver nitrate with thallium nitrate and of ammonium nitrate with thallium nitrate, having the compositions $Ag[Tl(NO_3)_2]$ and $NH_4[Tl(NO_3)_2]$; of these, four salts were investigated for the first time.

Saturated solutions were electrolyzed in electrolyzers of 100-300 ml capacity, at relatively low current densities from 12 to 20 $ma/cm^2$ and an electrode potential of 2-2.5 v. Platinum plates, 1 $cm^2$ in area, served as electrodes.

When the stated conditions are met, finely crystalline, black deposits with a metallic luster are produced in the form of a close-fitting film on the anode, from electrolytes without organic admixtures. The highest possible concentration of solutions and low current strength are essential. Otherwise, gas bubbles begin to appear at the anode together with the deposit, and the latter is obtained in an extremely fine, brownish form and does not adhere to the electrode.

We carefully washed the electrolyte from the shiny, black deposit obtained at the anode and dried the deposit to constant weight at 110-120°. It was very stable to washing with water and drying up to 170°. Concentrated sulfuric acid did not dissolve the deposit, and on heating, evolution of oxygen, which would have occurred in the case of peroxide formation at the anode, was not observed. The deposit was readily soluble at room temperature in concentrated and dilute hydrochloric acid without evolution of chlorine, and the precipitate described by Gallo and Cenni [9] was not formed at all.

The anode deposits were subjected to a detailed analytical determination of their content of thallium, total oxygen, and higher oxides, as well as any possible additional components.

Thallium was determined by two methods – precipitation as $Tl(OH)_3$ and precipitation as TlI. The total amount of oxygen contained in the anode deposit was determined by the method of reducing it with hydrogen and collecting the water formed. We determined the amount of oxygen in higher oxides, easily detached in the presence of any reducing agent, firstly by the usual method of reducing the oxides with oxalic acid and subsequently precipitating the excess acid as calcium oxalate monohydrate, and secondly by measuring the volume of oxygen evolved from the deposits on heating the latter at 700-750° in a current of carbon dioxide (used for removal of oxygen). The acid ions contained in the deposit were determined in each case by means of the appropriate reagents. The fluorine found in the deposit was quantitatively determined by the volumetric method through the reaction

$$AlCl_3 + 6NaF = Na_3[AlF_6] + 3NaCl.$$

The standard solutions of sodium fluoride and aluminum chloride were prepared by the method developed by I. M. Tananaev.

Average Results of Analyses of Deposits Obtained on Electrolysis of Thallium Salts

| Element determined | Found (in %) in anode deposit from: | | | | | | Calculated (in %) for | |
|---|---|---|---|---|---|---|---|---|
| | $TlNO_3$ | $Ag[Tl(NO_3)_2]$ | $NH_4[Tl(NO_3)_2]$ | TlF | $Tl_2SO_4$ | $Tl_2CO_3$ | $Tl_2O_3$ | $Tl_2O_3 \cdot HF$ |
| Thallium | | | | | | | | |
| a) determination as $Tl_2O_3$ | 89.24 | 89.26 | 89.33 | 85.79 | 87.34 | 89.10 | 89.49 | 85.78 |
| b) determination as TlI | — | — | — | — | 87.59 | 89.30 | — | — |
| Oxygen | | | | | | | | |
| a) total quantity | 10.42 | 10.49 | 10.51 | 10.14 | — | 10.54 | 10.51 | 10.07 |
| b) evolved on heating | — | — | — | — | 6.99 | 6.57 | 7.00 | — |
| c) participating in the oxidation of oxalic acid | 6.98 | 6.89 | 6.90 | — | 7.15 | 6.99 | 7.00 | — |
| Fluorine | — | — | — | 3.94 | — | — | — | 3.99 |
| Sulfate ion | — | — | — | — | 1.78 | — | — | — |
| $Tl_a/Tl_c$ ratio | 0.502 | 0.503 | 0.504 | 0.50 | 0.49 | 0.50 | 0.50 | 0.50 |

The analytical results are given in the summary table. From the data obtained it follows that anode deposits from the nitrate, the carbonate, and the complex salts consist only of thallium trioxide. The anode deposit from thallium fluoride contains fluorine. On the basis of analysis the formula $Tl_2O_3 \cdot HF$ should be assigned to it; this is in accord with cited data [10].

Analysis of the anode deposit from thallium sulfate showed the presence of sulfate ion in the amount of 1.78% on the average. The anode deposit obtained from thallous sulfate solutions apparently consists of thallium trioxide with an admixture of sulfate ion in some undetermined form.

For the purpose of a more accurate determination of the composition of the anode deposits obtained on electrolysis of thallous-salt solutions, X-ray analyses of all the anode deposits, as well as a parallel analysis of pure, chemically prepared thallic oxide, were conducted in the Laboratory of Dielectric Physics of the Physical Institute of the USSR Academy of Sciences. The purity of the orginal salts was checked by spectral

Fig. 1. X-ray diffraction pattern of chemically-prepared $Tl_2O_3$.

Fig. 2. X-ray diffraction pattern of anode deposit from $TlNO_3$.

Fig. 3. X-ray diffraction pattern of anode deposit from TlF.

Fig. 4. X-ray diffraction pattern of anode deposit from $Tl_2SO_4$.

Fig. 5. X-rya diffraction pattern of anode deposit from $Tl_2CO_3$.

analysis, which revealed only unweighable traces of Pb and Zn in the nitrate prepared by us from metallic thallium.

X-ray diffraction patterns of the anode deposits obtained on electrolysis of thallium nitrate and carbonate solutions and the X-ray pattern of chemically prepared thallium trioxide have identical lines, which exactly coincided when superposed.

X-ray diffraction patterns of the anode deposits from solutions of thallium fluoride and sulfate and X-ray patterns of thallic oxide chemically prepared from the salt have common lines corresponding to $Tl_2O_3$; besides, the X-ray patterns of these anode deposits contain many additional lines, which evidently belong to the fluoride and sulfate ions present in the deposits.

X-ray diffraction patterns of anode deposits are shown in Figures 1-5.

In order to confirm the composition of the deposits obtained on the anode we used not only analytical and X-ray methods, but also a method proposed earlier [11], which consists in determining the ratio of the quantity of thallium in the anode deposit ($Tl_a$) to the quantity of thallium which separated out at the cathode ($Tl_c$) during the same time. If a deposit containing two tervalent thallium atoms is formed on the anode as a result of the anodic oxidation of thallium from the univalent state to the tervalent, the total number of electrons lost by the thallium in oxidation at the anode is equal to four: $2Tl^{+} - 4e^{-} - 2Tl^{+++}$. At the cathode, then, four univalent thallium atoms may be reduced during the same time: $4Tl^{+} + 4e^{-} - 4Tl$. Therefore the ratio of the quantity of thallium deposited on the anode to the quantity of thallium deposited on the cathode, $Tl_a/Tl_c$, must be equal to 0.5. In a great number of experiments on the electrolysis of thallium salts we were able to confirm this ratio in all cases (see summary table).

## SUMMARY

1. It has been shown that in the electrolysis of solutions of thallous salts – the nitrate, fluoride, sulfate, and carbonate and complex salts of the compositions $Ag[Tl(NO_3)_2]$ and $NH_4[Tl(NO_3)_2]$ – black, extremely stable, finely-crystalline deposits, which have a metallic luster and closely fit the electrode, are obtained at the platinum anode. In the literature the electrolysis of solutions of thallium nitrate and sulfate, only, is described. Solutions of the other four salts were electrolyzed for the first time.

2. It has been shown that the anode deposit is thallium trioxide, $Tl_2O_3$. The deposit obtained from thallium sulfate solution contains an admixture of sulfate ion in the amount of 1.78%; the anode deposit from the fluoride solution has the composition $Tl_2O_3 \cdot HF$.

## LITERATURE CITED

[1] L. Shucht and Hutt, Zbl. 39, 121 (1880); Z. anal. Ch. 22, 490 (1883).

[2] F. Foerster, Z. Elektroch. 2, 653 (1897).

[3] M. E. Heiberg, Z. allg. anorg. Ch. 35, 347 (1903).

[4] W. Dieterle, Z. Elektroch. 29, 493 (1923).

[5] A. Gutbier and W. Dieterle, Z. Elektroch. 29, 457 (1923).

[6] I. Besson, C. r. 224, 1226 (1947); 225, 1154 (1947); 222, 28 (1946); Anal. Chem. Acta 3, 158 (1949).

[7] A. Lipchinskii, J. Analyt. Chem. 12, 83 (1957).*

[8] M. Centnerszwer and T. Trebaczkiewicz, Z. phys. Ch. 165, 367 (1933); J. Am. Chem. Soc. 55, 3065 (1933).

[9] G. Gallo and G. Cenni, Atti Linc. 5, 17, 276 (1908); Gazz. 35, 2 (1905).

[10] A. Jilek and Lukas, Collection Trav. Chim. Tchecoslov. 1, 417 (1929); Chem. Listy 24, 245, 223 (1930).

[11] M. S. Skanavi-Grigor'eva and I. L. Shimanovich, J. Gen. Chem. 24, 1490 (1954);* 26, 1540 (1956).*

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# IRREVERSIBLE-COMMON SYSTEM OF SODIUM AND POTASSIUM BUTYRATES AND THIOCYANATES

N. M. Sokolov and E. I. Pochtakova

The immediate task of the present work is to investigate the direction of the exchange reaction between sodium and potassium butyrates and thiocyanates in melts containing them. The given common system is one of a series of systems composed of salts of thiocyanic acid and of fatty acids; the over-all purpose of the study of these systems is to determine the dependence of the direction of the exchange reaction on the structure of the fatty-acid salt radical [1].

Potassium thiocyanate has a polymorphic transformation at 143° [2], whereas sodium thiocyanate, to judge from literature data [2], has no polymorphic transformations. An investigation by one of us [3] revealed that polymorphism occurs in the case of butyrates. Thus, sodium butyrate has transformations at 117, 232, 252, and 316°, and potassium butyrate at 190, 280-285, and 345°.

## EXPERIMENTAL

All the work was done by the visual-polythermic method, the usual procedure being employed. The temperature was measured with a nichrome-constantan thermocouple.

Commercial thiocyanate preparations were twice recrystallized, first from water and then from alcohol. Sodium and potassium butyrates were synthesized from the acid and C. P. bicarbonates according to directions published earlier [4]. The salts obtained were recrystallized from butanol. Melting points: sodium butyrates, 330°; potassium butyrate, 404°; sodium thiocyanate, 311°; potassium thiocyanate, 177°. In Table 1-3 all compositions are given in molar percentages, and the temperatures of formation of the first crystals are stated.

### Binary Sub-Systems

1. The NaCNS–KCNS system. This was first described as a system with eutectic melting [2]. According to our data, the two branches of the liquidus curve intersect at 126° and 74% KCNS (Table 1, Figure 1).

2. The $C_3H_7COONa$–$C_3H_7COOK$ system was investigated for the first time; it gives a continuous series of solid solutions (Table 1, Figure 1).

3. The NaCNS–$C_3H_7COONa$ system. This was described earlier by one of us [5]. The three branches of the liquidus curve intersect at the eutectic point 262° and 51.5% $C_3H_7COONa$, and the transition point, 268° and 68.5% $C_3H_7COONa$ (Table 1, Figure 1).

4. The KCNS–$C_3H_7COOK$ system. Investigated for the first time. Here complex formation takes place. The three branches of the liquidus curve intersect at the eutectic point, 170° and 6.5% $C_3H_7COOK$, and the transition point, 335° and 82% $C_3H_7COOK$. The composition $6C_3H_7COOK \cdot KCNS$ is proposed for the addition compound (Table 1, Figure 1).

### Diagonal Sections

The stable diagonal section KCNS–$C_3H_7COONa$. The phase diagram consists of two branches, which intersect at the eutectic point, 165° and 4% $C_3H_7COONa$ (Table 2, Figure 2).

TABLE 1

Binary Systems

| Na, K ∥ CNS | | Na, K ∥ $C_3H_7COO$ | | Na ∥ CNS, $C_3H_7COO$ | | K ∥ CNS, $C_3H_7COO$ | |
|---|---|---|---|---|---|---|---|
| KCNS (mol %) | temperature | $C_3H_7COOK$ (mol %) | temperature | $C_3H_7COONa$ (mol %) | temperature | $C_3H_7COOK$ (mol %) | temperature |
| 0 | 311° | 0 | 330° | 0 | 311° | 0 | 177° |
| 5 | 304 | 5 | 339 | 5 | 307 | 2.5 | 176 |
| 10 | 298 | 10 | 348 | 10 | 304 | 5 | 174 |
| 15 | 292 | 15 | 356 | 15 | 302 | 6.5 | 170 |
| 20 | 282 | 20 | 364 | 20 | 300 | 7.5 | 173 |
| 25 | 272 | 25 | 370 | 25 | 298 | 10 | 183 |
| 30 | 262 | 30 | 375 | 30 | 295 | 15 | 204 |
| 35 | 251 | 35 | 380 | 35 | 290 | 20 | 215 |
| 40 | 238 | 40 | 385 | 40 | 287 | 25 | 224 |
| 45 | 224 | 45 | 389 | 45 | 280 | 30 | 232 |
| 50 | 211 | 50 | 393 | 50 | 269 | 45 | 260 |
| 55 | 195 | 55 | 396 | 51.5 | 262 | 55 | 278 |
| 60 | 178 | 60 | 399 | 55 | 263 | 65 | 301 |
| 65 | 162 | 65 | 402 | 60 | 264 | 70 | 310 |
| 70 | 142 | 70 | 405 | 65 | 266 | 75 | 322 |
| 72.5 | 131 | 75 | 406 | 68.5 | 268 | 77.5 | 327 |
| 74 | 126 | 80 | 406 | 75 | 275 | 80 | 335 |
| 75 | 127 | 85 | 405 | 70 | 291 | 82 | 335 |
| 80 | 139 | 90 | 405 | 85 | 316 | 82.5 | 337 |
| 85 | 150 | 95 | 404 | 90 | 324 | 85 | 342 |
| 90 | 158 | 100 | 404 | 95 | 328 | 90 | 364 |
| 95 | 168 | | | 100 | 330 | 95 | 379 |
| 100 | 177 | | | | | 100 | 404 |

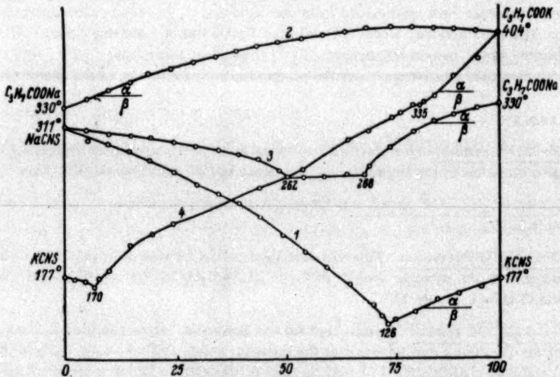


Fig. 1. Phase diagrams of binary systems. 1) NaCNS–KCNS, 2) $C_3H_7COONa$–$C_3H_7COOK$, 3) NaCNS–$C_3H_7COONa$, 4) KCNS–$C_3H_7COOK$.

The metastable diagonal section NaCNS–$C_3H_7COOK$. Potassium butyrate forms solid solutions with the exchange product ($C_3H_7COONa$). Therefore the phase diagram consists only of two branches, which intersect at 239° and 26% $C_3H_7COOK$ (Table 2, Figure 2).

## Internal Sections

In order to reveal the surface of crystallization of the system we investigated 20 internal sections, the disposition of which is given in Figure 3. Crystallization curves are shown in Figure 4.

TABLE 2

Diagonal Sections

| Stable diagonal section KCNS–$C_3H_7COONa$ | | Metastable diagonal section NaCNS–$C_3H_7COOK$ | | Stable diagonal section KCNS–$C_3H_7COONa$ | | Metastable diagonal section NaCNS–$C_3H_7COOK$ | |
|---|---|---|---|---|---|---|---|
| $C_3H_7COONa$ (mol %) | temperature | $C_3H_7COOK$ (mol %) | temperature | $C_3H_7COONa$ (mol %) | temperature | $C_3H_7COOK$ (mol %) | temperature |
| 0 | 177° | 0 | 311° | 45 | 263° | 50 | 267° |
| 2.5 | 169 | 5 | 302 | 50 | 265 | 55 | 272 |
| 4 | 165 | 10 | 292 | 60 | 273 | 60 | 278 |
| 5 | 176 | 15 | 280 | 65 | 278 | 65 | 285 |
| 10 | 217 | 20 | 260 | 70 | 285 | 70 | 297 |
| 15 | 237 | 25 | 242 | 75 | 295 | 75 | 317 |
| 20 | 248 | 26 | 239 | 80 | 307 | 80 | 336 |
| 25 | 254 | 30 | 247 | 85 | 318 | 85 | 348 |
| 30 | 259 | 35 | 252 | 90 | 326 | 90 | 364 |
| 35 | 262 | 40 | 257 | 100 | 330 | 95 | 387 |
| 40 | 264 | 45 | 265 | | | 100 | 404 |

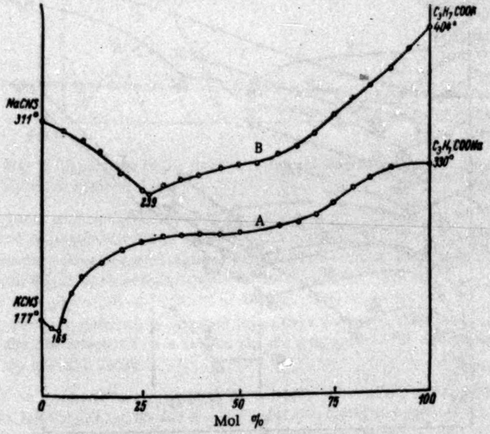
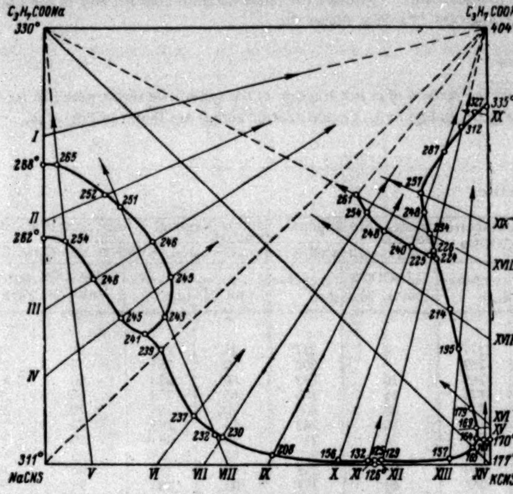


Fig. 2. Diagonal sections of the system. A) Stable diagonal section; B) metastable diagonal section.



C₃H₇COONa
330°
C₃H₇COOK
404°
335°
327
XX
312
287
257
261
254
248
246
234
226
240
225
224
XIX
XVIII
214
XVII
195
173
169
XVI
XV
170°
177°
I
288°
265
252
251
II
282°
254
246
248
243
III
245
243
241
239
IV
237
232
230
208
158
132
125
129
137
311°
NaCNS
V
VI
VII
VIII
IX
X
XI
126°
XII
XIII
XIV
KCNS

Fig. 3. Direction of internal sections.

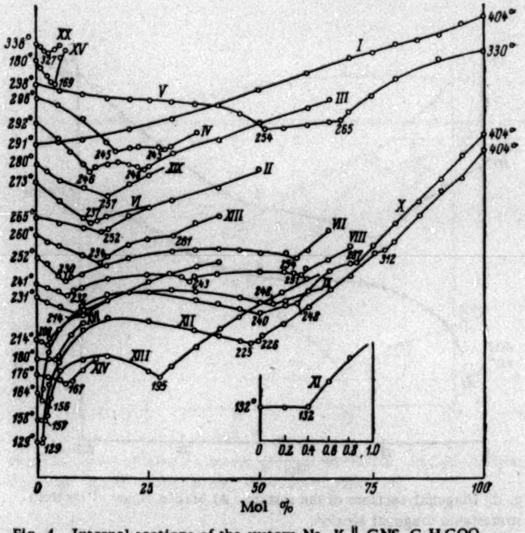


Fig. 4. Internal sections of the system Na, K ‖ CNS, $C_3H_7COO$.

## DISCUSSION

As a result of the investigation of binary sub-systems of the common system, diagonals, and 20 internal sections,the projection of the three-dimensional diagram was plotted on the square of composition. The system investigated is a diagonal, irreversible-common system, the equilibrium in which is shifted toward the stable salt pair $C_3H_7COONa$ and KCNS, which are not the most refractory components of the present system. Owing to the lack of data on heats of formation both for butyrates and for their additioncompounds, it is possible to judge whether the direction of the reaction corresponds to the conventional heat of reaction.

The surface of the liquidus of the system consists of the following fields; The field of solid solutions of the butyrates – 73.7% of the total surface (below 260° it breaks up into potassium butyrate and sodium butyrate fields); that of NaCNS – 13.2%; that of KCNS – 0.5%; that of the addition compound $6C_3H_7COOK \cdot KCNS$ – 6.7%; that of the addition compound $4C_3H_7COONa \cdot NaCNS$ – 5.9% (Figure 5).

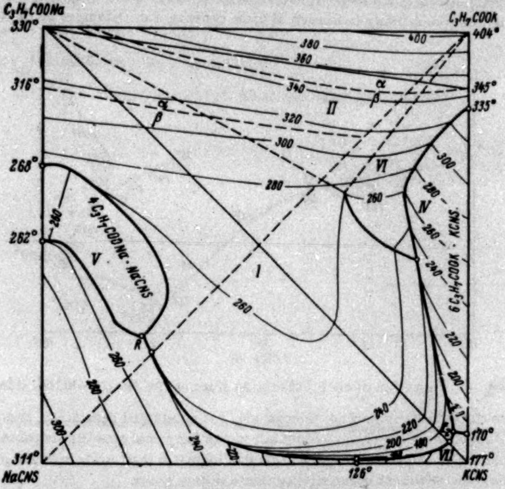


Fig. 5. Projection of the three-dimensional diagram of the system on the square of composition.

The stable diagonal section $C_3H_7COONa$–KCNS and the section passing from the hypothetical pole of the addition compound $6C_3H_7COOK \cdot KCNS$ to the $C_3H_7COONa$ vertex divide the entire surface of the square of the common system into three phase triangles: 1) $C_3H_7COONa$–NaCNS with the triple eutectic point $E_1$ and the transition point R; 2) KCNS–$6C_3H_7COOK \cdot KCNS$–$C_3H_7COONa$ with the triple eutectic point $E_2$; 3) $6C_3H_7COOK \cdot KCNS$–$C_3H_7COONa$–$C_3H_7COOK$ with the triple transition point P. In order to determine the temperature and composition of the triple invariant points more precisely, a projection of the cocrystallization lines was plotted on the NaCNS–KCNS side (Figure 6); the temperatures and compositions corresponding to the invariant points are given in Table 3.

Comparison of the results of investigation of the present system with systems investigated earlier – Na, K ‖ HCOO, CNS; Na,K ‖ $CH_3COO$, CNS and Na, K ‖ $C_2H_5COO$, CNS [1] – shows that in all these systems the equilibrium is irreversibly shifted toward the formation of potassium thiocyanate and the sodium salt of the fatty acid. Of the salts of the stable pair in these systems the most stable is the sodium salt of the fatty acid, which, as the number of carbon atoms in the salt molecule increases, drives the KCNS further back along the stable diagonal. Thus, in the system formed by formates the fraction of KCNS on the stable diagonal amounts

**TABLE 3**

Triple Invariant Points

| Designation of points | Temperature | Composition at the invariant point |
|---|---|---|
| $E_1$ | 125° | 73.6% KCNS, 0.4% $C_3H_7COONa$, 26% NaCNS |
| $R$ | 241 | 23% KCNS, 30% $C_3H_7COONa$, 47% NaCNS |
| $E_2$ | 164 | 93.5% KCNS, 2.5% $C_3H_7COONa$, 4% $C_3H_7COOK$ |
| $P$ | 234 | 52.5% KCNS, 12.5% $C_3H_7COONa$, 35% $C_3H_7COOK$ |

to 28.5%; in the acetate system it is 14.5%; in the propinate, 7.5%; in the butyrate, 4%. If A. P. Palkin [6] is followed further and the stable triangles in each of these systems, i.e., triangles of the type: sodium salt of the fatty acid–sodium thiocyanate–potassium thiocyanate, are considered separately, then, as is evident from Table 4, the area falling to the share of the sodium salt of the fatty acid steadily increases as the number of carbon atoms per molecule of the latter increases. All this indicates that as the number of carbon atoms in the salt molecule increases, the degree of irreversibility in the system grows.

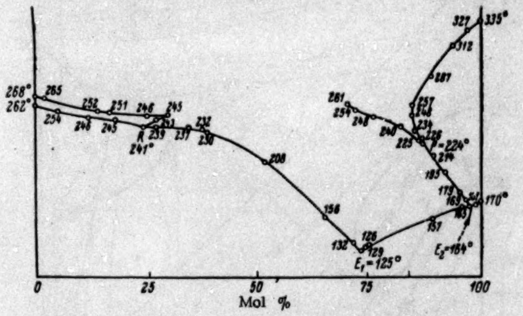


Fig. 6. Projection of cocrystallization lines on the NaCNS–KCNS side.

**TABLE 4**

Relative Sizes of Fields

| System | Size of field (in % of the total surface of the field of the stable triangle) | |
|---|---|---|
| | field of KCNS | field of sodium salt of fatty acid |
| Na, K ‖ HCOO, CNS | 12.3 | 40.9 |
| Na, K ‖ $CH_3COO$, CNS | 4.2 | 65.6 |
| Na, K ‖ $C_2H_5COO$, CNS | 2.2 | 73 |
| Na, K ‖ $C_3H_7COO$, CNS | 1.2 | 61 * |

In conclusion, we regard it as a pleasant duty to thank A. G. Bergman for valuable advice.

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*Part of the $C_3H_7COONa$ is used up in the formation of the addition compound $4C_3H_7COONa \cdot NaCNS$.

## SUMMARY

1. The irreversible-common system of sodium and potassium butyrates and thiocyanates has been investigated.

2. The liquidus curves of the binary systems $C_3H_7COONa-C_3H_7COOK$ and $KCNS-C_3H_7COOK$.

3. As the number of carbon atoms in the salt radical increases, the degree of irreversibility in systems formed by salts of a fatty acid and sodium and potassium thiocyanates grows.

## LITERATURE CITED

[1] N. M. Sokolov, Theses of the 3rd All-Union Conf. on Phys.-Chem. Analysis, Moscow (1955).*

[2] I. B. Vrzhesnevskii, J. Russ. Phys.-Chem. Soc. 43, 1368 (1911).

[3] N. M. Sokolov, Theses of Repts. to the Xth Sci. Session of the Smolensk Med. Inst. (1956).*

[4] N. M. Sokolov, J. Gen. Chem. 24, 1581 (1954).**

[5] N. M. Sokolov, J. Gen. Chem. 24, 1150 (1954).**

[6] A. P. Palkin, Bull. Sect. Phys.-Chem. Anal. Acad. Sci. USSR 18, 228 (1949).

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Smolensk Medical Institute.

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*In Russian.

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# TOWARD THE QUESTION OF CONTACT FUSION OF CRYSTALS

P. A. Savintsev and V. E. Avericheva

In a work by M. Kh. Gluzman and V. P. Rubtsova [1], devoted to contact fusion of three- and four-component organic systems giving eutectics, there are a number of errors which mislead the reader with regard to the present state of the problem.

The authors hold that contact fusion in ternary and quaternary eutectic systems may be observed on contact of a specimen of a binary (ternary) eutectic with a piece of a substance giving a ternary (quaternary) eutectic with the specimen. However, another method of detecting contact fusion of ternary (quaternary) eutectic systems has also been described [2]. Contact fusion occurs also on heating a mixture of powders of the three (four) components. In this case increase in the dispersity of the components lead to increase in the total contact surface among them, thereby facilitating contact fusion.

The authors write that contact fusion of ternary and quaternary eutectic systems was described by S. V. Avakian and N. F. Lashko [3] in 1949 and do not mention that it had already been described by D. D. Saratovkin and P. A. Savintsev [4] in 1947. Contact fusion of organic substances had been described even earlier [5].

The phenomenon of contact fusion may be explained [2] by the difference between interactions of homogeneous and heterogeneous atoms; in the solid state, interaction between homogeneous atoms predominates, whereas that between heterogeneous atoms predominates in the liquid state. The temperature of contact fusion is that temperature at which the transition from one type of particle interaction to the other takes place.

Temperature of Contact Fusion of Substances Forming Solid Solutions

| Component | | Melting point | | Temperature of contact fusion |
|---|---|---|---|---|
| A | B | $t_A$ | $t_B$ | |
| NaCl | KCl | 800° | 790° | 660° |
| KBr | NaBr | 768 | 770 | 670 |
| KCl | KBr | 790 | 768 | 750 |
| NaI | KI | 700 | 710 | 580 |
| KCl | NaBr | 790 | 770 | 646 |
| NaBr | NaI | 770 | 700 | 640 |
| NaBr | KI | 770 | 710 | 560 |

It might be supposed that we encounter a similar phenomenon not only in eutectic systems, but also in systems forming solid solutions. Therefore the phenomenon of contact fusion may be expected in this case as well. To confirm the above we performed experiments with the crystals listed in the table.

Crystals A and B were brought into contact and heated. As the temperature $\underline{t}^*$ was reached, liquid appeared at the point of contact. Our X-ray investigations of the solidified melts obtained in contact fusion have confirmed that we are dealing with solid solutions. The melt of the KCl-NaCl system is an exception. In this case the roentgenograms indicate a mixture of components. Thermal analysis of the KCl–NaCl system indicates solid solutions which separated into two phases at temperatures below 495°. Evidently this also explains the form of the KCl–NaCl system roentgenogram.

Substances forming solid solutions can diffuse into each other, which leads to their sintering at a temperature lower than the melting points of the components. In order to ascertain the effect of diffusion on contact fusion we held the specimens in contact at a temperature 50° below that of contact fusion for 10-20 hours; after this treatment we observed no sintering of the specimens. Evidently diffusion processes have no effect on the phenomenon of contact fusion of crystals.

The experiments which were performed provide grounds for the assertion that contact fusion occurs both in the case of substances forming eutectics and in that of substances forming solid solutions. The easy fusibility of the eutectics and solid solutions cannot be explained by the structural properties of the eutectic or solid solution. Therefore the temperature of contact fusion is a physical quantity determined by the disposition of adjacent particles with respect to one another.

## LITERATURE CITED

[1] M. Kh. Gluzman and V. P. Rubtsova, J. Gen. Chem. 27, 704 (1957).

[2] P. A. Savintsev, Bull. Tomsk Polytech. Inst. 68, No. 1 (1951).

[3] S. V. Avakian and N. F. Lashko, Proc. Acad. Sci. USSR, 65, 29 (1949).

[4] D. D. Saratovkin and P. A. Savintsev, Proc. Acad. Sci. USSR 58, 1943 (1947).

[5] D. D. Saratovkin and P. A. Savintsev, Proc. Acad. Sci. USSR 33, 303 (1941).

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# INVESTIGATION OF THE REACTION OF PHENYL-β-NAPHTHYLAMINE WITH ORGANIC ACIDS BY THE METHODS OF PHYSICO-CHEMICAL ANALYSIS

N. K. Tsvetkova and D. E. Dionis'ev

The introduction of a benzene nucleus into an aromatic-amine molecule markedly lowers its activity with respect to organic acids. It was of interest to ascertain how the replacement of one benzene nucleus in a secondary-amine molecule by a naphthalene nucleus affects its ability to react with organic acids.

The reaction of phenyl-β-naphthylamine with organic acids has not been studied before by anyone.

## EXPERIMENTAL

Phenyl-β-naphthylamine was recrystallized several times from ethyl alcohol and dried in a desiccator in a current of warm air; m.p. 106.3°. Trichloroacetic acid of C. P. grade was distilled three times and kept in sealed ampules; m.p. 59°, b. p. 197°. Salicylic acid of C. P. grade was purified by repeated recrystallization and had m. p. 159.8°. Succinic acid of C. P. grade had m. p. 184.5° after recrystallization. Adipic acid of C. P. grade had m. p. 151°.

Measurements of viscosity, density, and electrical conductivity were performed in a glycerol thermostat which permitted maintenance of the temperature within a ±0.1° range. The mixtures were prepared by the method of separate weighed portions. Concentrations were calculated in molar percentages; viscosities were expressed in centipoises.

1. The phenyl-β-naphthylamine–trichloroacetic acid system was studied by us with regard to melting point, viscosity, density, and specific electrical conductivity (Figure 1).

The liquidus curve has a maximum corresponding to 50 mol. % phenyl-β-naphthylamine, which indicates the formation in the solid phase of a compound with equimolar composition, $\beta\text{-}C_{10}H_7NHC_6H_5 \cdot CCl_3COOH$, having m.p. 94.5°. Eutectic points; 88.5° and 60 mol. % phenyl-β-naphthylamine, and 33° and 12 mol. % of the latter.

The viscosity and density of this system were studied at 90, 100, and 110°. At 90 and 100° these properties, as well as the electrical conductivity, could not be investigated completely, since mixtures with a high-phenyl-β-naphthylamine content were not supercooled at the stated temperatures. The density curves were convex to the concentration axis, which indicates the absence of shrinkage in the system. The viscosity curve at 90° has a maximum corresponding to 40 mol. % phenyl-β-naphthylamine in the mixture. As the temperature rises, the maximum is displaced toward higher concentrations of trichloroacetic acid, i. e., the less viscous component. On the curves of the absolute temperature coefficient the maximum is retained. Thus the form of the viscosity curves indicates that the components are combined in the liquid phase. The shift of the maximum on the viscosity curves toward the less viscous component indicates, in the opinion of V. V. Udovenko [1], that the components form a new compound in the liquid phase. It is difficult to judge the composition of the compound from the position of the maximum in the given case.

The electrical conductivity of the mixtures at first increases slowly, but then, beginning at 40 mol. % phenyl-β-naphthylamine, rises sharply, passes through a maximum corresponding to 10 mol.% phenyl-β-naph-

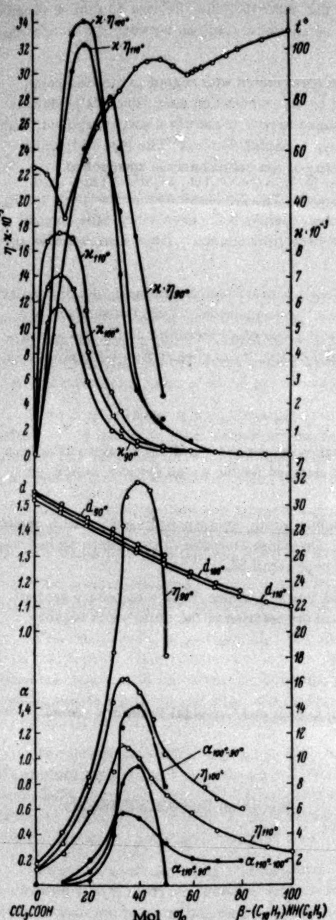

Fig. 1. Phenyl-β-naphthylamine–trichloroacetic acid system. Liquidus (t), viscosity, (η), density (d), and specific (χ) and corrected (η, χ) electrical conductivity curves.

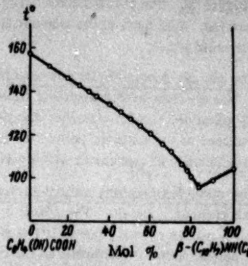

Fig. 2. Liquidus curve of the phenyl-β-naphthyl-amine–salicylic acid system.

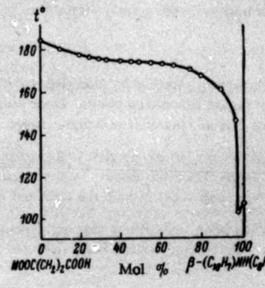

Fig. 3. Liquidus curve of the phenyl-β-naphthyl-amine–succinic acid system.

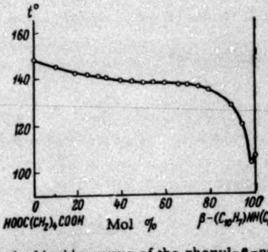

Fig. 4. Liquidus curve of the phenyl-β-naphthyl-amine–adipic acid system.

thylamine, and falls sharply to the value for pure trichloroacetic acid. On correcting the electrical conductivity for viscosity the maximum is only slightly displaced. According to M. I. Usanovich [2] curves having this form indicate an acid-base reaction in the system, although the position of the maximum does not correspond to the composition of the compound.

2. The phenyl-β-naphthylamine–salicylic acid system was investigated by us with regard only to melting points (Figure 2). The two branches of the curve intersect at the eutectic point, 98° and 85 mol. % phenyl-β-naphthylamine. The form of the liquidus curve indicates that no chemical reaction between the components occurs in the solid phase.

3. The phenyl-β-naphthylamine–succinic acid system was investigated with regard to melting points (Figure 3). The succinic acid branch is a curve, slightly inclined to the composition axis, which falls abruptly at 80 mol.% phenyl-β-naphthylamine; the phenyl-β-naphthylamine branch is merely a small fragment. Both branches intersect at the eutectic point, 103° and 98 mol. % phenyl-β-naphthylamine. The type of liquidus curve is characteristic of systems in which partial mutual miscibility of the components is approached.

4. The phenyl-β-naphthylamine–adipic acid system (Figure 4). The liquidus curve is extremely similar to that of the preceding system. The adipic acid branch is a sloping, slightly bent curve which falls abruptly from 80 mol. % to the eutectic point (104° and 99 mol. % phenyl-β-naphthylamine). Here, also, we have an approach to partial mutual miscibility of the components.

The investigation revealed that phenyl-β-naphthylamine reacts with trichloroacetic acid like diphenylamine. In the other systems studied there is no chemical reaction between the components. Thus, introduction of a naphthalene nucleus in the place of a benzene ring in a molecule of a secondary aromatic amine has almost no effect on the character of the reaction with organic acids, and the capacity of phenyl-β-naphthylamine for complex formation is still greatly diminished.

## SUMMARY

1. The systems formed by phenyl-β-naphthylamine with salicylic, succinic, and adipic acids have been studied with regard to melting points. Phase diagrams have been obtained for the stated systems, which indicate that there is no chemical reaction between the components.

2. The sytem formed by phenyl-β-naphthylamine with trichloroacetic acid has been studied with regard to melting points, viscosity, density, and electrical conductivity. On phase diagrams of the system an indication that the components react in both the solid and liquid phases has been obtained.

3. It has been established that replacement of one benzene ring in a molecule of a secondary aromatic amine by a naphthalene nucleus is not reflected in the character of the reaction of the amine with organic acids.

## LITERATURE CITED

[1] V. V. Udovenko. Works of the Conf. on the Viscosity of Liquids and Colloidal Solutions. Acad. Sci. USSR Press, 89 (1944).*

[2] M. I. Usanovich and V. Dulova, J. Gen. Chem. 17, 669 (1947).

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*In Russian.

# COMPOUNDS OF CADMIUM AND MERCURY HALIDES WITH NICOTINE

I. A. Kondrashov and S. F. Babak

It was shown earlier by us [1-3] that halides of mercury, zinc, and cadmium form the following types of addition compounds with nicotine: $MeX_2 \cdot C_{10}H_{14}N_2$, $MeX_2 \cdot 2C_{10}H_{14}N_2$, $HMeX_3 \cdot C_{10}H_{14}N_2$, and $H_2MeX_4 \cdot$ $\cdot C_{10}H_{14}N_2$, depending on the conditions of reaction. According to their composition and properties, the last two types of compounds apparently are salts of nicotine and the corresponding complex halide acids of mercury, zinc, and cadmium, some of which are known in the free state [4].

The present report is a continuation of investigations of complex compounds of mercury and cadmium halides of the last three types, which are not described in the literature. Compounds of mercuric chloride and bromide with nicotine, having the composition $MeX_2 \cdot 2C_{10}H_{14}N_2$, are readily formed on mixing stoichiometric quantities of the component substances in acetone solution.

Compounds with cadmium bromide and iodide, having the same composition, are formed like the mercury compounds, but they can be prepared also by solution of the salts in pure, hot nicotine; however, cadmium chloride reacts with nicotine only when the latter is heated.

The compounds were prepared with a slight excess of nicotine and with energetic stirring of the reaction mixture; they were washed several times with ether in a Schott filter, dried in a desiccator, and analyzed.

The compound $CdBr_2 \cdot C_{10}H_{14}H_2 \cdot HBr$ was formed by mixing aqueous solutions of equimolar quantities of its components. The precipitated crystals were dissolved in the mother liquor on heating, and the solution was concentrated with carbolene (karbolen)and filtered. The filtrate was drawn off by suction, and the crystals were washed in the filter and dried in a desiccator. In preparing the compound $CdI_2 \cdot C_{10}H_{14}N_2 \cdot HI$ the starting materials consisted of equimolar quantities of cadmium oxide and nicotine and 3 mol. of hydriodic acid.

The compound $CdBr_2 \cdot C_{10}H_{14}N_2 \cdot 2HBr$ was readily formed when equimolar quantities of aqueous solutions of cadmium bromide and nicotine were vigorously mixed in a strongly acidic hydrobromic acid medium. The compound $CdI_2 \cdot C_{10}H_{14}N_2 \cdot 2HI$ was prepared from equimolar quantities of cadmium oxide dissolved in excess hydriodic acid in nicotine [sic]. In both cases the crystals were filtered out from the mother liquor, washed with a little water, and dried in air and then in a desiccator.

Nicotine, acetone, $CdBr_2$, and $HgI_2$ of C. P. grade were used; $HgCl_2$ and $HgBr_2$ were prepared from HgO by treatment with acids, followed by sublimation. $CdCl_2$ was prepared from CdO by treatment with acid, followed by recrystallization and then dehydration at 120°.

Cadmium and mercury were determined gravimetrically as $CdSO_4$ and HgS. Halogens and nicotine were determined in the same way as before [3].

$HgCl_2 \cdot 2C_{10}H_{14}N_2$ – fine, white crystals. M. p. 107-110° (dec.). Yield 85%.

Found %: $C_{10}H_{14}N_2$ 55.22, 53.90, 53.80; Cl 12.80, 11.68, 11.60; Hg 34.00, 33.68. $HgCl_2 \cdot 2C_{10}H_{14}N_2$.
Calculated %: $C_{10}H_{14}N_2$ 54.43; Cl 11.90; Hg 33.67.

$HgBr_2 \cdot 2C_{10}H_{14}N_2$ – fine, white crystals. M. p. 114-117° (dec.). Yield 83%.

Found %: $C_{10}H_{14}N_2$ 44.75, 44.45, 44.42; Br 23.52, 23.66, 23.48; Hg 31.91. $HgBr_2 \cdot 2C_{10}H_{14}N_2$.
Calculated %: $C_{10}H_{14}N_2$ 44.78; Br 23.33; Hg 31.89.

$HgI_2 \cdot 2C_{10}H_{14}N_2$ was prepared from $HgI_2 \cdot C_{10}H_{14}N_2$ [5] by dissolving the latter in hot nicotine. When this solution was cooled, fine, brown crystals separated out, which after filtration, washing with acetone to remove nicotine, and drying gave a white powder with m.p. 127-128° (dec.). Yield 62%.

Found %: $C_{10}H_{14}N_2$ 42.24, 41.86; I 32.55, 33.26, 32.75; Hg 25.61, 25.04. $HgI_2 \cdot 2C_{10}H_{14}N_2$. Calculated %: $C_{10}H_{14}N_2$ 41.62; I 32.60; Hg 25.78.

$CdCl_2 \cdot 2C_{10}H_{14}N_2$ – a white, crystalline substance which began to decompose at 90° and melted at 125° with decomposition. Yield about 92%.

Found %: $C_{10}H_{14}N_2$ 63.64, 63.85, 63.60; Cl 13.44, 13.51; Cd 22.00, 22.23. $CdCl_2 \cdot 2C_{10}H_{14}N_2$. Calculated %: $C_{10}H_{14}N_2$ 63.88; Cl 13.97; Cd 22.14.

$CdBr_2 \cdot 2C_{10}H_{14}N_2$ a white, crystalline substance with m.p. 135-136°. (dec.). Yield 86%.

Found %: $C_{10}H_{14}N_2$ 54.45, 54.56; Br 26.63, 26.45; Cd 18.97, 19.11, 18.99. $CdBr_2 \cdot 2C_{10}H_{14}N_2$. Calculated %: $C_{10}H_{14}N_2$ 54.36; Br 26.79; Cd 18.84.

$CdI_2 \cdot 2C_{10}H_{14}N_2$ –a white, crystalline substance which melted at 130° (dec.). Yield 91%.

Found %: $C_{10}H_{14}N_2$ 47.02, 46.94; I 36.10, 36.73; Cd 16.08, 15.95, 16.22. $CdI_2 \cdot 2C_{10}H_{14}N_2$. Calculated %: $C_{10}H_{14}N_2$ 46.97; I 36.76; Cd 16.28.]

$CdBr_2 \cdot C_{10}H_{14}N_2 \cdot HBr$ –white crystals, m.p. 169-171° (dec.).

Found %: $C_{10}H_{14}N_2$ 31.56, 31.52; Br 46.59, 46.65; Cd 21.87, 21.75. $CdBr_2 \cdot C_{10}H_{14}N_2 \cdot HBr$. Calculated %: $C_{10}H_{14}N_2$ 31.46; Br 46.52; Cd 21.80.

$CdI_2 \cdot C_{10}H_{14}N_2 \cdot HI$ – white, slightly yellowish crystals. M. p. 203-205° (dec.). Yield about 100%.

Found %: $C_{10}H_{14}N_2$ 24.15, 24.48; I 58.21, 58.18; Cd 17.05, 17.27. $CdI_2 \cdot C_{10}H_{14}N_2 \cdot HI$. Calculated %: $C_{10}H_{14}N_2$ 24.70; I 58.01; Cd 17.13.

$CdBr_2 \cdot C_{10}H_{14}N_2 \cdot 2HBr$ – white crystals. M. p. 205-208° (dec.). Yield 71%.

Found %: $C_{10}H_{14}N_2$ 27.49, 27.83, 27.54; Br 53.58, 53.72; Cd 18.59, 18.33, 18.71. $CdBr_2 \cdot C_{10}H_{14}N_2 \cdot 2HBr$. Calculated %: $C_{10}H_{14}N_2$ 27.19; Br 53.61; Cd 18.86.

$CdI_2 \cdot C_{10}H_{14}N_2 \cdot 2HI$ – slightly yellowish crystals. M. p. 209-210° (dec.). Yield 38%.

Found %: $C_{10}H_{14}N_2$ 20.38, 20.74, 20.26; I 64.40, 63.53; Cd 14.18, 14.12, 14.38. $CdI_2 \cdot C_{10}H_{14}N_2 \cdot 2HI$. Calculated %: $C_{10}H_{14}N_2$ 20.67; I 64.74; Cd 14.33.

We determined the solubilities, molar electrical conductivities, and pH values in water at 25° of the compounds of cadmium halides with nicotine, and also the previously described [1, 3] compounds of mercury and zinc halides with nicotine, having the composition $H_2MeX_4 \cdot C_{10}H_{14}N_2$, which are listed in the table.

As is evident from the data of the table, the compound $ZnI_2 \cdot C_{10}H_{14}N_2 \cdot 2HI$ has a pH of 6.31. Other zinc and cadmium compounds of the same type have pH values between 3 and 4. This is apparently due to the fact that the complex compound $ZnI_2 \cdot C_{10}H_{14}N_2 \cdot 2HI$ is more stable and it decomposes in aqueous solution to a lesser degree than other zinc and cadmium compounds of this type.

The molecular weights of the compounds $ZnCl_2 \cdot 2C_{10}H_{14}N_2$ and $ZnBr_2 \cdot 2C_{10}H_{14}N_2$ in acetone were also ebullioscopically determined.

Found : M 446. $ZnCl_2 \cdot 2C_{10}H_{14}N_2$. Calculated: M 460.55. Found: M 573. $ZnBr_2 \cdot 2C_{10}H_{14}N_2$. Calculated: M 549.38.

It must be assumed that these substances are addition products.

The melting points of compounds containing two molecules of acid are higher than those of compounds containing one molecule of acid, and compounds of both types have higher melting points than compounds of the type $MeX_2 \cdot 2C_{10}H_{14}N_2$, obtained from organic solvents. The melting points of compounds of zinc with nicotine are higher than those of the corresponding compounds of cadmium and mercury with nicotine. Compounds containing bromine are higher-melting than chlorine compounds, whereas iodine compounds are higher-melting than the corresponding bromine compounds in some cases, but lower-melting in others.

The solubility of compounds of the type $MeX_2 \cdot C_{10}H_{14}N_2 \cdot 2HX$ in water at 25° decreases as the atomic numbers of the metal and halogen decrease.

| Compound | Solubility (in %) | Dilution (1 mole/ 1000 liters) | |
|---|---|---|---|
| | | electrical conductivity | pH |
| $ZnCl_2 \cdot C_{10}H_{14}N_2 \cdot 2HCl \cdot H_2O$ | 50.66 | 620 | 3.24 |
| $ZnBr_2 \cdot C_{10}H_{14}N_2 \cdot 2HBr$ | 30.10 | 613 | 3.26 |
| $ZnI_2 \cdot C_{10}H_{14}N_2 \cdot 2HI$ | 5.70 | 450 | 6.31 |
| $CdCl_2 \cdot C_{10}H_{14}N_2 \cdot 2HCl \cdot H_2O$ | 46.44 | 604 | 3.29 |
| $CdBr_2 \cdot C_{10}H_{14}N_2 \cdot 2HBr$ | 9.30 | 581 | 3.28 |
| $CdI_2 \cdot C_{10}H_{14}N_2 \cdot 2HI$ | 0.87 | 581 | 3.80 |
| $HgCl_2 \cdot C_{10}H_{14}N_2 \cdot 2HCl \cdot H_2O$ | — | 450 | — |
| $HgBr_2 \cdot C_{10}H_{14}N_2 \cdot 2HBr$ | — | 450 | — |

The molar electrical conductivity and pH indicate that in solution these compounds are completely decomposed to the original components with subsequent dissociation and hydrolysis.

## SUMMARY

1. The prepared complex compounds of nicotine with cadmium bromide and iodide and the corresponding hydrohalic acids, of the type $MeX_2 \cdot C_{10}H_{14}N_2 \cdot 2HX$, are salts of nicotine and complex halide acids of cadmium, completely dissociated in aqueous solutions. It has been established that the solubility in water of compounds of this type decreases as the atomic number of the element increases.

2. Complex compounds of mercury and cadmium halides with nicotine, of the type $MeX_2 \cdot 2C_{10}H_{14}N_2$, have been prepared.

3. Tne complex compounds $CdBr_2 \cdot C_{10}H_{14}N_2 \cdot HBr$ and $CdI_2 \cdot C_{10}H_{14}N_2 \cdot HI$, have been prepared.

## LITERATURE CITED

[1] S. F. Babak and I. A. Kondrashov. Report on the Scientific Works of Members of the D. I. Mendeleev All-Union Chem. Soc. [VKhO], No. 3, 18 (1953).

[2] S. F. Babak and R. Kh. Zamanov. Report on the Scientific Works of Members of the D. I. Mendeleev All-Union Chem. Soc. [VKhO], No. 4, 50 (1953).

[3] S. F. Babak and I. A. Kondrashov, J. Gen. Chem. 24, 1759 (1954).*

[4] A. Verner. Modern Views in the Field of Inorganic Chemistry. 105 (1936).

[5] A. A. Shmuk, Chemistry of Tobacco and Makhorka, 93 (1938).**

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Samarkand State Medical Institute

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*Original Russian pagination. See C.B. Translation.

**In Russian.

# LETTERS TO THE EDITOR

## STUDY OF THE WALLACH REARRANGEMENT AND RELATED REACTIONS*

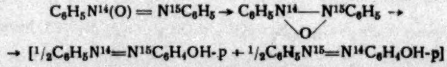
M. M. Shemiakin, V.I. Maimind and B. K. Vaichunaite

The mechanism of the azoxy combination reaction was recently elucidated by us [1] by means of $N^{15}$, and it was established that this process goes through a stage of formation of intermediate dioxy compounds. At present we have used $N^{15}$ for the study of various isomerizations of azoxy compounds – the Wallach rearrangement and related reactions.

For this purpose $C_6H_5N^{15}H_2$ and $o\text{-}O_2N^{14}C_6H_4CHO$ , synthesized from $C_6H_5N^{14}(O)=N^{15}C_6H_5$ (cf. [2, 3]), was rearranged to o- and p-hydroxyazobenzenes under varying conditions. The isotopic composition of the nitrogens in the azoxybenzene was determined by bromination followed by reductive cleavage [1], whereas that in the hydroxyazobenzenes was determined by reduction with tin in concentrated hydrochloric acid at 85-90°, aniline and aminophenols being isolated in the form of the acetyl derivatives.

It was found that in the presence of chlorosulfonic acid (-8°, 1 hour; see [4] for conditions of isolation) the rearrangement of azoxybenzene to p-hydroxyazobenzene is accompanied by complete equalization of the isotopic composition of both nitrogens.

On treatment of azoxybenzene with 83% sulfuric acid without heating (22-24°, 8.5 days) the same results were obtained; at the same time it was shown that the observed equalization of activity takes place in the rearrangement process itself and not before it, since the isotopic composition of the unreacted azoxybenzene remained practically unchanged. These results cannot be explained by the hypotheses on the mechanism of rearrangements of this kind, advanced earlier in the literature [4]. Under the described conditions, apparently, the initial stage of the process is the isomerization of the original azoxybenzene to the symmetrical oxide.



$$C_6H_5N^{14}(O)=N^{15}C_6H_5 \rightarrow C_6H_5N^{14}\underset{\diagdown O \diagup}{\text{——}}N^{15}C_6H_5 \rightarrow$$
$$\rightarrow [{}^1/_2C_6H_5N^{14}=N^{15}C_6H_4OH\text{-}p + {}^1/_2C_6H_5N^{15}=N^{14}C_6H_4OH\text{-}p]$$

On heating azoxybenzene with 83% sulfuric acid (90°, 8 minutes) only partial (85%) equalization of activity occurred, a higher $N^{15}$ concentration being found at that N atom in p-hydroxyazobenzene, which was attached to the hydroxyl-bearing benzene ring; at the same time the unreacted azoxybenzene was recovered unchanged. Therefore under these conditions the conversion of azoxybenzene to p-hydroxyazobenzene exceeds by two different routes; in one of them (the main route; the scheme is given above) the rearrangement goes through a stage of oxide formation, whereas in the other (the secondary route; the scheme is given below) this stage is bypassed.

$$C_6H_5N^{14}(O)=N^{15}C_6H_5 \rightarrow C_6H_5N^{14}=N^{15}C_6H_4OH\text{-}p$$

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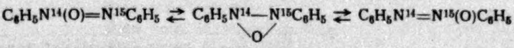
* Presented at the General Assembly of the Division of Chemical Sciences of the USSR Academy of Sciences, Moscow, December 19, 1957.

In a rearrangement carried out under the influence of ultraviolet light (65 hours at 30-45° in 85% alcohol) [5] there was almost no equalization of the isotopic composition of the nitrogens in the o-hydroxyazobenzene, a higher $N^{15}$ concentration being found at the nitrogen atom attached to the hydroxyl-bearing benzene ring. In this case the isomerization process bypasses the stage of oxide formation.

$$C_6H_5N^{14}(O){=}N^{15}C_6H_5 \rightarrow C_6H_5N^{14}{=}N^{15}C_6H_4OH\text{-}o$$

At the same time a considerable (about 15%) degree of equalization of the isotopic composition of the nitrogens in the unreacted azoxybenzene was found. Under the influence of ultraviolet light, apparently, azoxybenzene can be reversibly isomerized very slowly from one form to the other through the intermediately formed oxide:



$$C_6H_5N^{14}(O){=}N^{15}C_6H_5 \rightleftarrows C_6H_5\underset{\diagdown O \diagup}{N^{14}{-}N^{15}}C_6H_5 \rightleftarrows C_6H_5N^{14}{=}N^{15}(O)C_6H_5$$

On heating with acetic anhydride (4 hours, 230-240°) the rearrangement of azoxybenzene to o-hydroxyazobenzene takes place in the same way as under the influence of ultraviolet light, but in this case no change at all is observed in the isotopic composition of the nitrogens in the unreacted azoxybenzene.

## LITERATURE CITED

[1] M. M. Shemiakin, V. I. Maimind, and B. K. Vaichunaite, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1260 (1957).*

[2] A. Reissert and F. Hemmer, Ber. 59, 351 (1926).

[3] L. E. Behr, J. Amer. Chem. Soc. 76, 3672 (1954).

[4] V. O. Lukashevich and G. N. Kurdiumova, J. Gen. Chem. 18, 1963 (1948).

[5] G. Badger and R. G. Buttery, J. Chem. Soc. 1954, 2243.

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# SYNTHESIS OF L-ACETYLALANINE FROM D,L-ALANINE

V. B. Spirichev and L. A. Shchukina

As is known, one of the most successful preparative methods for the separation of racemic amino acids into antipodes is the method proposed by Greenstein and co-workers [1, 2]. This method is based on the ability of acylase to deacylate only the L-forms of various N-acylated α-amino acids, leaving the D-forms of the acylamino acids practically unaffected.

It was shown by us that the process of deacylation of amino acids by acylase is reversible and, under certain conditions, L-acylamino acids can be synthesized from L- or D,L-amino acids by means of it. Thus, on treatment with the acylase, obtained from pig kidneys [2, 3], for 24 hours in the presence of 2 moles of sodium acetate (pH 7.8, 37°) D,L-alanine is converted to L-acetylalanine with a yield of about 15%.

The acylating ability of acylase, which we discovered, can be made the basis of a method for synthesizing L-acylamino acids directly from racemic amino acids.

## LITERATURE CITED

[1] V. E. Price and J. P. Greenstein, J. Biol. Ch. 175, 969 (1948).

[2] S. M. Birnbaum, L. Levintow, R. B. Kingsley, J. P. Greenstein, J. Biol. Ch. 194, 453 (1952).

[2] CH'i Cheng-wu and V.N. Orekhovich, Biochemistry 22, 838 (1957).

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# SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

| | |
|---|---|
| FIAN | Phys. Inst. Acad. Sci. USSR. |
| GDI | Water Power Inst. |
| GITI | State Sci.-Tech. Press |
| GITTL | State Tech. and Theor. Lit. Press |
| GONTI | State United Sci.-Tech. Press |
| Gosenergoizdat | State Power Press |
| Goskhimizdat | State Chem. Press |
| GOST | All-Union State Standard |
| GTTI | State Tech. and Theor. Lit. Press |
| IL | Foreign Lit. Press |
| ISN (Izd. Sov. Nauk) | Soviet Science Press |
| Izd. AN SSSR | Acad. Sci. USSR Press |
| Izd. MGU | Moscow State Univ. Press |
| LEIIZhT | Leningrad Power Inst. of Railroad Engineering |
| LET | Leningrad Elec. Engr. School |
| LETI | Leningrad Electrotechnical Inst. |
| LETIIZhT | Leningrad Electrical Engineering Research Inst. of Railroad Engr. |
| Mashgiz | State Sci.-Tech. Press for Machine Construction Lit. |
| MEP | Ministry of Electrical Industry |
| MES | Ministry of Electrical Power Plants |
| MESEP | Ministry of Electrical Power Plants and the Electrical Industry |
| MGU | Moscow State Univ. |
| MKhTI | Moscow Inst. Chem. Tech. |
| MOPI | Moscow Regional Pedagogical Inst. |
| MSP | Ministry of Industrial Construction |
| NII ZVUKSZAPIOI | Scientific Research Inst. of Sound Recording |
| NIKFI | Sci. Inst. of Modern Motion Picture Photography |
| ONTI | United Sci.-Tech. Press |
| OTI | Division of Technical Information |
| OTN | Div. Tech. Sci. |
| Stroiizdat | Construction Press |
| TOE | Association of Power Engineers |
| TsKTI | Central Research Inst. for Boilers and Turbines |
| TsNIEL | Central Scientific Research Elec. Engr. Lab. |
| TsNIEL-MES | Central Scientific Research Elec. Engr. Lab.—Ministry of Electric Power Plants |
| TsVTI | Central Office of Economic Information |
| UF | Ural Branch |
| VIESKh | All-Union Inst. of Rural Elec. Power Stations |
| VNIIM | All-Union Scientific Research Inst. of Meteorology |
| VNIIZhDT | All-Union Scientific Research Inst. of Railroad Engineering |
| VTI | All-Union Thermotech. Inst. |
| VZEI | All-Union Power Correspondence Inst. |

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. — Publisher.

# A COMPARISON OF THE RATE OF HYDROGEN EXCHANGE WITH PROTOPHILIC SOLVENTS

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The work of our laboratory has shown that parallel investigations of hydrogen exchange reactions with acid and basic solvents allow us to draw very full conclusions as to the reactivity of organic substances and also permit an explanation of the rules of hydrogen exchange [1]. For an explanation of the mechanism of the exchange, it is interesting to carry out a reaction of deuterium exchange of dissolved substances with solvents of the same chemical nature, but which differ in their protolytic activity and physical constants. Among the latter, the dielectric constants (DC) of the solvents and dipole moments (DM) of their molecules have particular value. The polarity of the molecules is shown by the reaction between the dissolved substances and the solvents, and the value of the dielectric constant of the latter affects the state of protolytic equilibrium in the solution on which, in turn, depends the rate of hydrogen exchange.

Our work presents a comparison of the rate of hydrogen exchange of a series of substances with liquid ammonia and other protophilic solvents: anhydrous hydrazine, ethylenediamine, and ethanol amine.

TABLE 1

Physical Constants of the Solvents

| | Temp. | | | $\kappa_{H_2O}$ | Ionic conductivity | DC 25° | DM $\mu \cdot 10^{18}$ |
|---|---|---|---|---|---|---|---|
| | melting | boiling | critical | | | | |
| $NH_3$ | −77.7° | −33.35° | 132° | $2 \cdot 10^{-5}$ | $10^{-33}$ | 16 | 1.46 |
| $NH_2NH_2$ | 2 | 113.5 | 158 | $3 \cdot 10^{-6}$ | $10^{-25}$ | 52 | 1.84 |
| $NH_2CH_2CH_2NH_2$ | 11 | 116.2 | — | $1 \cdot 10^{-4}$ | — | 14 | 1.94 |
| $NH_2CH_2CH_2OH$ | 10.5 | 172.2 | — | $3 \cdot 10^{-5}$ | $10^{-6}$ | 38 | 2.27 |
| $H_2O$ | 0 | 100.0 | 374 | — | $10^{-14}$ | 80 | 1.84 |

Table 1 gives some constants for $NH_3$, $N_2H_4$, $NH_2CH_2CH_2NH_2$, $NH_2CH_2CH_2OH$ (for comparison we give the corresponding values for $H_2O$). The ionization constants in water solution ($K_{H_2O}$) give some idea of the relative basicity of the substances but they may be wrong with reference to the anhydrous solvents.

## Obtaining Anhydrous Deuterium Solvents*

Anhydrous hydrazine was obtained by the method of Brown and Welsh [2] by ammonolysis of hydrazine sulfate by liquid ammonia for which we used the somewhat modified extractor of V. A. Pleskov [3] (Fig. 1). The siphon which we connected to the receiving flask permitted us to draw off the anhydrous hydrazine into a glass ampoule attached by Wood metal to a steel connection. The latter was screwed onto a metallic apparatus supplied with a valve [4] for the addition of liquid deuteroammonia obtained as described in [5]. The exchange

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*In this work substances are called deuterium substituted when they have different deuterium contents; the formulas for the deuterium compounds have a conditional character.

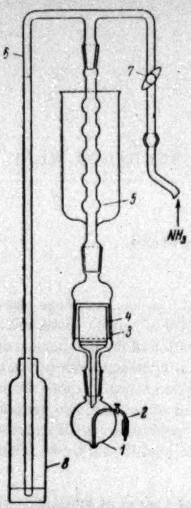

Fig. 1. Extractor.
1) Flask; 2) siphon; 3) conical connection; 4) funnel with glass filter; 5) condenser; 6) barometer tube; 7) stopcock; 8) mercury reservoir.

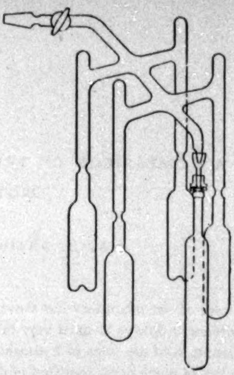

Fig. 2. Multiple collector for distilling deuterium solvents.

reaction between $N_2H_4$ and $ND_3$ occurred instantaneously [6]. After the deuteroammonia was distilled off, the deuterohydrazine was twice distilled over BaO in a high vacuum a multiple collector (Fig. 2) and was collected in ampoules with concave thinned bottoms, which were detached.

Anhydrous ethylenediamine was obtained in an analogous manner by ammonolysis of ethylenediamine sulfate. The latter was prepared by neutralizing a commercial 20% aqueous solution of ethylenediamine by concentrated sulfuric acid, evaporating the water, and drying the salt at 120° in a stream of nitrogen or hydrogen. Deuterium was introduced into the anhydrous ethylenediamine as described above.

Ethanol amine, a commercial preparation, was distilled over sodium. We collected the middle fraction for our work. Deuterium was introduced in the same way as for the other solvents.

## Isotopic Analysis of the Solvents

Isotopic analysis of deuterium substituted ammonia, hydrazine, ethylenediamine, and ethanol amine consisted in burning 0.1-0.2 g of the substance and determining by the micro method [7] the deuterium concentration in the water obtained by the laboratory method of burning and purifying [8].

Hydrazine, ethylenediamine and ethanol amine were burned in a stream of oxygen by the method of rapid burning of organic substances worked out in this laboratory. Burning of ammonia was carried out over copper oxide at 700-750°. The water obtained by burning ammonia was distilled through the same oven with copper oxide and then purified.*

Examples of the analyses: deuterium substituted ammonia – 20.8, 20.5, 20.4, average 20.6 at. %; deuterium substituted hydrazine – 37.5, 37.7, 38.1, 37.9, average 37.8 at. %. Accuracy of the analysis ±1-2%.

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*This method of isotopic analysis of ammonia, worked out by the authors of this paper, is used in all the work of our laboratory for the study of the reactions of hydrogen exchange with liquid deuteroammonia.

## Method of Carrying out Experiments on Isotope Exchange

Solutions of organic substances in deuterohydrazine were prepared in a high vacuum. The collector (Fig. 3) was joined by a ground glass joint to the high vacuum apparatus. In an ampoule sealed to the collector was placed a weight of substance sufficient for obtaining about 0.2 g of water from it by burning, and on the support of vessel 1, joined to the connection, was placed ampoule 2 which was filled with deuterohydrazine. After pumping out, stopcock 5 was closed, the collector was disconnected from the high vacuum system and lightly shaken to break the bottom of ampoule 2. The whole ampoule was evenly cooled with liquid nitrogen including the sample of substance, then into each ampoule was distilled 5-6 grams of deuterohydrazine; the ampoule was detached and placed in a thermostat. After remaining in the thermostat, the ampoule was placed in a mixture of carbon dioxide and acetone and was opened; the hydrazine was distilled off in a high vacuum. The organic substance was washed with ammonia, alcohol, or water (depending on its properties) to guarantee full removal of deuterohydrazine. After the substance was dried in a vacuum, its constants were determined (melting point, refractive index), and then the substance was dried, the water which it formed was purified, and its concentration of deuterium was determined by the micromethod.

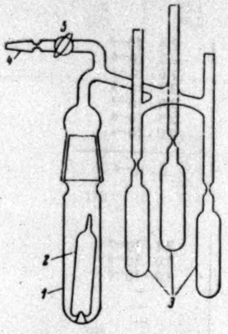

Fig. 3. Collector for preparing solutions in hydrazine.
1) Vessel with support;
2) ampoule with thin bottom, filled with solvent; 3) ampoule with substance; 4) joint for uniting to the vacuum apparatus; 5) stopcock.

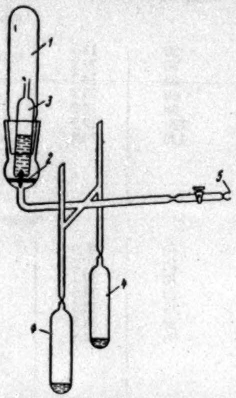

Fig. 4. Collector for preparing solutions with ethylenediamine.
1) Vessel; 2) support; 3) ampoule with solvent; 4) ampoule with substance;
5) joint for uniting with vacuum apparatus.

The solution of organic substances in deuteroethylenediamine was also prepared in a high vacuum. We introduced small changes in the construction of the apparatus which permitted flowing and not distilling the deuteroethylenediamine onto the sample of substance, which greatly shortened the experiment (10-15 min) at room temperature. In the collector used for this purpose (Fig. 4) vessel 1 was rotated 180° with respect to the ampoule. When the ampoule with the deuteroethylenediamine was placed on the support of vessel 1 and broken, the collector was twisted to pour the ethylenediamine into these ampoule, which was removed and placed in the thermostat. Separation of the substance from ethylenediamine in each case was different and was determined by the individual peculiarities.

The experiments with ethanol amine were carried out without special precautions. Ethanol amine was added to a weight of substance in air; the ampoule was pumped out and sealed. After the experiments the substance was separated from the ethanol amine by pouring into water, and filtering.

**TABLE 2**

**Results of Experiments on Isotopic Exchange**

| $\tau$ min | $C_s^\circ$ | $C_c^\circ$ | $C_c$ | $\alpha_p$ | $k(sec^{-1})$ |
|---|---|---|---|---|---|
| Fluorene–ammonia, 25° | | | | | |
| 30 | 13.5 | — | 0.48 | 0.4 | $1.4 \cdot 10^{-4}$ |
| 30 | 29.2 | — | 1.65 | 0.6 | $2.2 \cdot 10^{-4}$ |
| 60 | 13.3 | — | 1.10 | 0.8 | $1.6 \cdot 10^{-4}$ |
| 60 | 29.2 | — | 2.96 | 1.0 | $2.2 \cdot 10^{-4}$ |
| 60 | 29.2 | — | 3.50 | 1.2 | $2.0 \cdot 10^{-4}$ |
| 120 | 19.9 | — | 1.78 | 1.4 | $2.0 \cdot 10^{-4}$ |
| 120 | 29.2 | — | 4.03 | 1.4 | $2.0 \cdot 10^{-4}$ |
| | | | | Average | $2 \cdot 10^{-4}$ |
| Fluorene–ethylenediamine, 25° | | | | | |
| 10 | 39.0 | — | 5.48 | 1.4 | $2.4 \cdot 10^{-3}$ |
| 10 | 17.1 | — | 2.66 | 1.5 | $3.0 \cdot 10^{-3}$ |
| 10 | 17.1 | — | 2.62 | 1.5 | $3.0 \cdot 10^{-3}$ |
| 15 | 14.5 | — | 2.27 | 1.6 | — |
| 15 | 14.5 | — | 2.27 | 1.6 | — |
| 30 | 14.5 | — | 2.52 | 1.7 | — |
| 60 | 14.5 | — | 2.58 | 1.8 | — |
| | | | | Average | $3 \cdot 10^{-3}$ |
| Fluorene–ethanol amine, 25° | | | | | |
| 15 | — | 3.11 | 2.58 | — | $2.2 \cdot 10^{-4}$ |
| 15 | — | 3.11 | 2.48 | — | $2.5 \cdot 10^{-4}$ |
| 15 | — | 3.11 | 2.48 | — | $2.5 \cdot 10^{-4}$ |
| 30 | — | 3.11 | 2.00 | — | $2.4 \cdot 10^{-4}$ |
| 30 | — | 5.00 | 2.75 | — | $3.0 \cdot 10^{-4}$ |
| 30 | 56.7 | — | 4.21 | 0.74 | $2.9 \cdot 10^{-4}$ |
| 90 | 7.8 | — | 0.88 | 1.12 | $1.7 \cdot 10^{-4}$ |
| | | | | Average | $2 \cdot 10^{-4}$ |
| Triphenylmethane–ammonia, 120° | | | | | |
| 105 hrs | 29.2 | — | 0.16 | 0.09 | $3 \cdot 10^{-7}$ |
| 105 " | 29.2 | — | 0.12 | 0.07 | $2 \cdot 10^{-7}$ |
| 168 " | 29.2 | — | 0.18 | 0.10 | $2 \cdot 10^{-7}$ |
| 168 " | 29.2 | — | 0.16 | 0.09 | $2 \cdot 10^{-7}$ |
| 168 " | 29.2 | — | 0.17 | 0.09 | $2 \cdot 10^{-7}$ |
| | | | | Average | $2 \cdot 10^{-7}$ |
| Triphenylmethane–hydrazine, 120° | | | | | |
| 76 hrs | 36.8 | — | 1.30 | 0.6 | $(3 \cdot 10^{-6})$ |
| 96 " | 27.7 | — | 0.75 | 0.4 | $(2 \cdot 10^{-6})$ |
| 105 " | 34.2 | — | 1.70 | 0.8 | $(5 \cdot 10^{-6})$ |

TABLE 2 (continued)

| $\tau$, min | $C_s^0$ | $C_c^0$ | $C_c$ | $\alpha_p$ | k (sec$^{-1}$) |
|---|---|---|---|---|---|
| 168 | 31.1 | — | 1.08 | 0.6 | $(2 \cdot 10^{-6})$ |
| 168 | 31.1 | — | 1.14 | 0.6 | $(2 \cdot 10^{-6})$ |
| 168 | 31.1 | — | 1.10 | 0.6 | $(2 \cdot 10^{-6})$ |
| 200 | 36.8 | — | 1.51 | 0.7 | $(2 \cdot 10^{-6})$ |
| | | | | Average | $2 \cdot 10^{-6}$ |
| Triphenylmethane-ethylenediamine, 120° | | | | | |
| 50 | 39.0 | — | 0.58 | 0.2 | $2 \cdot 10^{-6}$ |
| 79 | 39.0 | — | 0.97 | 0.4 | $2 \cdot 10^{-6}$ |
| 80* | 29.4 | — | 0.49 | 0.3 | $1 \cdot 10^{-6}$ |
| 91 | 43.2 | — | 1.07 | 0.4 | $2 \cdot 10^{-6}$ |
| 112* | 29.4 | — | 0.66 | 0.4 | $1 \cdot 10^{-6}$ |
| | | | | Average | $2 \cdot 10^{-6}$ |
| Triphenylmethane-ethanol amine, 120° | | | | | |
| 103 | 56.7 | — | 0.57 | 0.16 | $5 \cdot 10^{-7}$ |
| 121 | 19.7 | — | 0.18 | 0.15 | $4 \cdot 10^{-7}$ |
| 124 | 56.7 | — | 0.84 | 0.24 | $6 \cdot 10^{-7}$ |
| 157 | 19.7 | — | 0.28 | 0.23 | $5 \cdot 10^{-7}$ |
| | | | | Average | $5 \cdot 10^{-7}$ |
| 100 | — | 0.67 | 0.57 | — | $4 \cdot 10^{-7}$ |
| 100 | — | 0.67 | 0.57 | — | $4 \cdot 10^{-7}$ |
| 109 | — | 5.27 | 4.69 | — | $3 \cdot 10^{-7}$ |
| 162 | — | 5.27 | 4.27 | — | $4 \cdot 10^{-7}$ |
| 162 | — | 5.27 | 4.44 | — | $3 \cdot 10^{-7}$ |
| | | | | Average | $4 \cdot 10^{-7}$ |
| Diphenylmethane-ammonia, 120° | | | | | |
| 200 | 90.9 | — | 0.06 | 0.008 | $6 \cdot 10^{-9}$ |
| 200 | 90.9 | — | 0.07 | 0.009 | $7 \cdot 10^{-9}$ |
| | | | | Average | $7 \cdot 10^{-9}$ |
| Diphenylmethane-hydrazine, 120° | | | | | |
| 168 | 31.1 | — | 0.46 | 0.2 | $(2 \cdot 10^{-7})$ |
| 200 | 36.8 | — | 0.77 | 0.3 | $(2 \cdot 10^{-7})$ |
| 200 | 36.8 | — | 0.74 | 0.2 | $(2 \cdot 10^{-7})$ |
| 200 | 36.8 | — | 0.55 | 0.2 | $(2 \cdot 10^{-7})$ |
| | | | | Average | $2 \cdot 10^{-7}$ |

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*Experiments were carried out with deuteroethylene diamine preparations repeatedly distilled over metallic potassium.

TABLE 2 (continued)

| $\tau$ sec | $C_s^0$ | $C_c^0$ | $C_c$ | $\alpha_p$ | k ($sec^{-1}$) |
|---|---|---|---|---|---|
| Diphenylmethane-ethylenediamine, 120° | | | | | |
| 65 | 43.6 | — | 0.16 | 0.04 | $1 \cdot 10^{-7}$ |
| 84 | 43.6 | — | 0.20 | 0.06 | $1 \cdot 10^{-7}$ |
| 112 | 40.9 | — | 0.28 | 0.08 | $1 \cdot 10^{-7}$ |
| | | | | Average | $1 \cdot 10^{-7}$ |
| Quinaldine-ethylenediamine, 120° | | | | | |
| 79 | 22.3 | — | 2.30 | 0.9 | $1 \cdot 10^{-6}$ |
| 109 | 42.8 | — | 5.27 | 1.1 | $1 \cdot 10^{-6}$ |
| 151 | 42.8 | — | 6.50 | 1.4 | $1 \cdot 10^{-6}$ |
| | | | | Average | $1 \cdot 10^{-6}$ |
| Quinaldine-ethanol amine, 120° | | | | | |
| 5 | 56.7 | — | 2.05 | 0.3 | $0.7 \cdot 10^{-5}$ |
| 7.5 | 56.7 | — | 2.45 | 0.4 | $0.6 \cdot 10^{-5}$ |
| 10 | 19.7 | — | 1.00 | 0.5 | $0.5 \cdot 10^{-5}$ |
| 15 | 19.7 | — | 1.58 | 0.7 | $0.6 \cdot 10^{-5}$ |
| 5 | — | 1.08 | 0.89 | — | $1 \cdot 10^{-5}$ |
| 6 | — | 1.08 | 0.81 | — | $1 \cdot 10^{-5}$ |
| 12 | — | 1.08 | 0.67 | — | $1 \cdot 10^{-5}$ |
| 12 | — | 1.08 | 0.70 | — | $1 \cdot 10^{-5}$ |
| 109 | — | 1.08 | 0.10 | — | — |
| 162 | — | 1.08 | 0.07 | — | — |
| 162 | — | 1.08 | 0.07 | — | — |
| | | | | Average | $8 \cdot 10^{-6}$ |

The experiments on isotopic exchange with liquid deuteroammonia were carried out using the method worked out and often tested in our laboratory [4-9].

## Characteristics of the Preparations

Fluorene. Twice recrystallized from alcohol. M. p. 115°. Deuterofluorene* was obtained by isotopic exchange with $ND_3$. $C_s^0$ = 17.3 at. %, $C_c$ = 3.11 at. %, $\alpha_p$ = 1.8. Recrystallized from alcohol. M. p. 115°. Deuterium entered the methylene group. Triphenylmethane, Eastman Kodak preparation. M. p. 92°. Deuterotriphenylmethane* was obtained by decomposing $(C_6H_5)_3CK$ with heavy water. The salt was obtained by dissolving triphenylmethane in a mixture of $NH_3 + KNH_2$. Recrystallized from alcohol. M. p. 93°. The deuterium entered the methine group. Diphenylmethane from the Kharkov Khimreaktiv Factory. M. p. 26.5°. Quinaldine was vacuum distilled, $n^{20}D$ 1.6110. Picrate m. p. 193.5°. Deuteroquinaldine* substituted by deuterium in the methyl group was obtained by short isotopic exchange with a 0.1 N solution $KND_2$ in $ND_3$. $C_s$ = 5.85 at. %, $C_c$ = 1.08 at. %, $\alpha_p$ = 1.3. Twice redistilled in vacuum, $n^{20}D$ 1.6099.

## Determination of Rate-Constant of Isotopic Exchange

The results of the experiments on exchange are given in Table 2 where: $\tau$ is duration of experiment, $C_s^0$ is deuterium concentration in the solvent, $C_c^0$ is deuterium concentration in the compound before the experiment,

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*See the note on page 1762. The abbreviations ($C_s^0$, $C_c$, $\alpha_p$) are explained below.

$C_c$ the deuterium concentration in the compound after the experiment, $\alpha_p$ the number of exchanged hydrogen atoms by distribution coefficient of deuterium between compound and solvent, k the rate constant calculated by the equation of the first order.

The values of k obtained in this work do not pretend to accuracy. The values of k obtained in the experiments with hydrazine have a purely conditional character and are placed in parentheses, since the experiments were carried out in a heterogeneous system because of the poor solubility of the organic substances in hydrazine.

The solubility of the organic substances with which this work was carried out in ethylenediamine was considerably better than in ammonia and ethanol amine. Solution of triphenylmethane and especially fluorene went slowly; this somewhat altered the results of the experiments on exchange. With a weight of compound in all cases of about 0.25 g, the weight of deuteroammonia and ethanol amine was about 15 g, of deuteroethylenediamine about 5 g, of deuterohydrazine, about 11 g. All the substances with which the work was carried out were not changed chemically during the exchange reaction, as indicated by the constancy of their constants before and after the experiments.

## Measurement of the Rate of Isotopic Exchange in the Presence of Catalysts

Comparison of the catalytic activity of basic catalysts in the studied solvents and comparison of the rate of hydrogen exchange in different solvents with the same basic catalyst could be a further step in explaining the mechanism of the reaction of isotopic exchange of hydrogen.

Usually in the reaction of alkali metals with solvents, bases are obtained. Thus, alkali hydroxides, alcoholates and amides of the metals are formed in the reaction between the metals and, respectively, water, alcohol, and ammonia. Ethanol amine reacts with alkali metals to form $NH_2CH_2CH_2OK$ and $NH_2CH_2CH_2ONa$ which are easily soluble in it. In the reaction of alkali metals with anhydrous hydrazine unstable hydrazides are formed.

When anhydrous ethylenediamine is added in a vacuum to metallic potassium, the metal becomes blue on the surface and over several hours forms a blue solution. The solution is formed only under conditions of very careful drying of the ethylenediamine by repeatedly distilling it in a vacuum over metallic potassium. Potassium and sodium amides are poorly soluble in anhydrous ethylenediamine.* The color of the solutions became successively violet, yellow-green, and brown. The solution catalyzed the reverse reaction. Thus, at room temperature after 18 days there occurred almost full exchange of hydrogen in naphthalene and after 5 days half the atoms of hydrogen in its molecule had exchanged.

$C_2H_5OK$ and $NH_2C_2H_4OK$ were also very weakly soluble in ethylenediamine.

Attempts to prepare a 0.1 N solution of $C_2H_5OK$ in ethylenediamine led to formation of a yellow solution, but most of the $C_2H_5OK$ remained undissolved. Experiments on the exchange of hydrogen in triphenylmethane with this solution showed that the methine atom exchanged hydrogen already in 15 min even at 25°, while without a catalyst the exchange became noticeable only at 120° ($k = 2 \cdot 10^{-6}$, see Table 2).

Analogous results were obtained with 0.1 N solutions of $H_2NCH_2CH_2OK$ in ethylenediamine.

The same bases, but dissolved correspondingly in ethanol amine and ethyl alcohol showed a much lower catalytic activity. This follows from the results of Table 3 and of the experiments of E. N. Zviagintseva [11] which showed that at 120° a 1 N solution of $C_2H_5OK$ in $C_2H_5OD$ caused hydrogen exchange in triphenylmethane with a rate of $3 \cdot 10^{-5}$ $sec^{-1}$.

## DISCUSSION OF RESULTS

The results of measuring the rate constants of hydrogen exchange are given in Table 4.

As Table 4 shows, hydrogen exchange with deuterohydrazine and deuteroethylenediamine occurs more rapidly than with deuteroammonia. The results of the experiments with hydrazine are particularly convincing because the exchange of hydrogen between triphenyl and diphenylmethane and hydrazine, is distinction from ammonia, takes

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* $KNH_2$, $C_2H_5OK$, and $NH_2C_2H_4OK$ were obtained by reaction of the metal with the corresponding solvent and after evaporation of the solvent, the dry residue was treated in a vacuum with ethylenediamine.

TABLE 3

Hydrogen Exchange with Ethanol Amine with a $NH_2C_2H_4O^-$ Catalyst

| τ hrs. | $C_s^*$ | $C_c^*$ | $C_c$ | $\alpha_p$ | k(sec$^{-1}$) |
|---|---|---|---|---|---|
| Fluorene, 0.1 N $NH_2C_2H_4OK$, 25° | | | | | |
| 0.25 | — | 5.00 | 0.41 | — | $2.8 \cdot 10^{-3}$ |
| 0.25 | — | 5.00 | 0.50 | — | $2.3 \cdot 10^{-3}$ |
| 0.50 | — | 5.00 | 0.29 | — | $1.6 \cdot 10^{-3}$ |
| | | | | Average | $2 \cdot 10^{-3}$ |
| Triphenylmethane, 0.1 N $NH_2C_2H_4OK$, 120° | | | | | |
| 5 | — | 2.02 | 1.41 | — | $2.0 \cdot 10^{-5}$ |
| 10 | — | 2.02 | 0.97 | — | $2.0 \cdot 10^{-5}$ |
| 15 | — | 2.02 | 0.89 | — | $1.5 \cdot 10^{-5}$ |
| 12 | 7.84 | — | 0.32 | 0.65 | $2.8 \cdot 10^{-5}$ |
| | | | | Average | $2 \cdot 10^{-5}$ |
| Triphenylmethane, 0.01 N $NH_2C_2H_4OK$, 120° | | | | | |
| 15 | — | 1.85 | 1.47 | — | $4 \cdot 10^{-6}$ |
| 10 | — | 1.85 | 1.65 | — | $3 \cdot 10^{-6}$ |
| 9 | — | 1.85 | 1.74 | — | $2 \cdot 10^{-6}$ |
| 7.3 | — | 5.27 | 4.57 | — | $6 \cdot 10^{-6}$ |
| 6.3 | — | 5.27 | 4.56 | — | $6 \cdot 10^{-6}$ |
| 6 | — | 5.27 | 5.05 | — | $2 \cdot 10^{-6}$ |
| 6 | — | 5.27 | 5.05 | — | $2 \cdot 10^{-6}$ |
| | | | | Average | $4 \cdot 10^{-6}$ |

TABLE 4

Rate Constants of Hydrogen Exchange

| Substance | k (sec$^{-1}$) (120°) | | | |
|---|---|---|---|---|
| | $ND_3$ | $N_2D_4$ | $ND_2C_2H_4ND_2$ | $ND_2C_2H_4OD$ |
| Fluorene** | $2 \cdot 10^{-4}$ *** | — | $3 \cdot 10^{-3}$ | $2 \cdot 10^{-4}$ |
| Triphenylmethane | $2 \cdot 10^{-7}$ | $(2 \cdot 10^{-6})$ | $2 \cdot 10^{-6}$ | $4 \cdot 10^{-7}$ |
| Diphenylmethane | $7 \cdot 10^{-9}$ | $(2 \cdot 10^{-7})$ | $1 \cdot 10^{-7}$ | — |
| Quinaldine | $7 \cdot 10^{-8}$ **** | — | $1 \cdot 10^{-6}$ | $8 \cdot 10^{-6}$ |

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*In the experiments with fluorine, the rate constant was measured at 25°.

**The rate constants obtained in [10] are lower, evidently because of the incomplete solubility of fluorene which was not noticed since the experiments were carried out in metal ampoules.

***Measured by E. N. Zviagintseva [11].

place in a heterogeneous system. The more rapid exchange of deuterium with hydrazine, a weaker base, than with ammonia is evidently related to the fact that the DC of hydrazine is 3 times greater than the DC of ammonia and its molecules are more polar.

The DC of ammonia and ethylenediamine are very close. Therefore the greater rate of exchange (by 10-15 times) with the second solvent must naturally be ascribed to its very protophilic nature. It is possible that the greater polarity of the ethylenediamine molecule also plays an important part.*

Deuterium exchange with ethanol amine shows characteristic peculiarities. The hydrogen of the methylene group of fluorene and the methine group of triphenylmethane exchanges with ethanol amine at about the same rate as with liquid ammonia, while the hydrogen of the methyl groups of quinaldine exchanges with ethanol amine more than twice as fast as with ammonia. In order to understand the reason for such contradictory results, we had to compare the rate of exchange in these substances with ammonia and ethanol. It has been shown [11] that hydrogen exchange between liquid ammonia and fluorene occure 6 times faster than with alcohol, while exchange of quinaldine with alcohol is faster than with ammonia. This was explained by different mechanisms of hydrogen exchange in these compounds.

The presence of two functional groups in the ethanol amine molecule permits it to act in two ways. We assume that in isotopic exchange of hydrogen in the $CH_2$ groups of fluorene, in the first step the amino group nitrogen of ethanol amine is the proton acceptor, while in the reaction with quinaldine a hydrogen bond is formed between the quinaldine nitrogen atom and the hydroxyl group of the ethanol amine, and the nitrogen acquires a positive charge. This leads to a decreased electron density on the carbon atom with which the methyl group is united, and in turn this eases the protonization of the hydrogen atom in the latter. We may think that the nitrogen atom of another ethanol amine molecule acts as proton acceptor. The greater protophilic character of ethanol amine as compared to quinaldine, which we must assume to play the part of acceptor in exchange in alcohol solution, is the reason for the fact that the rate of the exchange reaction in ethanol amine ($k = 8 \cdot 10^{-6}$) and in ammonia ($k = 7 \cdot 10^{-8}$) differs more than in alcohol ($k = 7 \cdot 10^{-7}$) and ammonia.

Table 5 gives the rate constants for the exchange of hydrogen in the methine group of triphenylmethane with the solvents and catalysts which interest us.

TABLE 5

Rate of Hydrogen Exchange in Triphenylmethane

| Solvent | Catalyst | Temperature | k ($sec^{-1}$) |
|---|---|---|---|
| Ethanol amine | — | 120° | $4 \cdot 10^{-7}$ |
| Ethylenediamine | — | 120 | $2 \cdot 10^{-6}$ |
| Ethanol amine | $NH_2C_2H_4OK$, ~0.01 N | 120 | $3 \cdot 10^{-6}$ |
| Ethanol amine | $NH_2C_2H_4OK$, ~0.1 N | 120 | $2 \cdot 10^{-5}$ |
| Ethylenediamine | $NH_2C_2H_4OK$, $<0.1$ N | 25 | $>10^{-3}$ |
| Ethanol | $C_2H_5OK$, 1 N | 120 | $3 \cdot 10^{-5}$ |
| Ethylenediamine | $C_2H_5OK$, $<0.1$ N | 25 | $>10^{-3}$ |

As the results in Table 5 show, the rate constants for the exchange reaction with ethylenediamine are about 5 times greater than with ethanol amine. At the same time, if the same catalyst ($NH_2C_2H_4OK$) is dissolved in these two solvents, the difference in rate constants is not less than 4-5 times, if we calculate that the experiments with ethylenediamine were carried out at a temperature 95° lower than those with ethanol amine.

A similar picture is found in comparing the rate of the exchange reactions which are catalyzed by alcoholates in ethanol and ethylenediamine.

Thus, a change in solvent can be very strongly reflected in the catalytic activity of the same base** in the reaction of isotopic exchange of hydrogen. It is interesting to compare with this the finding made in another study [11], that potassium hydroxide causes metallation of hydrocarbons dissolved in liquid ammonia.

We hope to study the rate of the exchange reactions catalyzed by the same base and in different solvents.

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*We once more emphasize the very conditional and unreliable estimates of the relative strengths of the solvents as based on the $K_{H_2O}$ values, which we must use because of the absence of reliable methods of comparison.

**We assume that the degree of transformation of alcoholate into $NH_2C_2H_4NH^-$ is very slight, since ethylenediamine is much more strongly basic than alcohol.

We express thanks to Iu. Bakshi who participated in carrying out the experiments with solutions in ethylenediamine in the absence of catalysts.

## SUMMARY

1. We have described the preparation of anhydrous deuterium substituted hydrazine, ethylenediamine, and ethanol amine, methods for their isotopic analysis, and the performance of experiments on isotopic exchange of hydrogen with them.

2. We have measured the rate of isotopic exchange of hydrogen in fluorene, triphenylmethane, diphenylmethane, and quinaldine with these solvents and with liquid ammonia.

3. We have discussed the reasons for the high rate of hydrogen exchange with hydrazine and ethylenediamine compared to liquid ammonia.

4. The peculiarities of deuterium exchange with ethanol amine have been explained by the fact that it can act as a donor and an acceptor of protons (deuterons).

5. We have measured the rate of isotopic exchange of hydrogen in triphenylmethane with ethylenediamine with catalysis by ions of $C_2H_5O^-$ and $NH_2C_2H_4O^-$, and also with ethanol amine with catalysis by $NH_2C_2H_4O^-$ ions. We have shown that the catalytic activity of a base depends in very great degree on the nature of the solvent.

## LITERATURE CITED

[1] A. I. Shatenshtein, Ukrain. Zhur. 22, 3 (1956); A. I. Shatenshtein and E. A. Iakovleva, DAN SSSR 105, 1024 (1955).

[2] A.Brown and T. Welsh, J. Am. Chem. Soc. 33, 1728 (1911).

[3] V. A. Pleskov, Zhur. Fiz. Khim. 12, 255 (1938).

[4] A. I. Shatenshtein, Zhur. Fiz. Khim. 15, 246 (1941).

[5] G. S. Landsberg, A. I. Shatenshtein, and others, Optics and Spectroscopy 1, 34 (1956).

[6] P. C. Cross and P. A. Leighton, J. Am. Chem. Soc. 60, 981 (1938).

[7] A. I. Shatenshtein and Ia. M. Varshavskii, Zhur. Anal. Khim 11, 746 (1956).*

[8] A. I. Shatenshtein and others, Isotopic Analysis of Water, Izd. AN SSSR (1957).**

[9] A. I. Shatenshtein and E. A. Izrailevich, Zhur. Fiz. Khim. 28, 3 (1954).

[10] A. I. Shatenshtein and Iu. P. Vyrskii, Zhur. Fiz. Khim. 25, 1206 (1951).

[11] A. I. Shatenshtein and E. N. Zviagintseva, DAN SSSR 117, 852 (1957).*

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# STUDIES OF THE REACTIONS OF TITANIUM TETRACHLORIDE WITH ESTERS OF MONOBASIC ACIDS

## XII. THE DECOMPOSITION OF THE COMPOUNDS $TiCl_4 \cdot$ESTER

Iu. A. Lysenko and O. A. Osipov

In our previous investigations [1-6] we established that titanium tetrachloride dissolves in esters of monobasic acids to form compounds of the composition $TiCl_4 \cdot E$ and $TiCl_4 \cdot 2E$ (where E is a molecule of ester); the product $TiCl_4 \cdot E$ is stable in the liquid phase and exists without change over a wide temperature interval. We did not find formation in the liquid phase of the compound $2TiCl_4 \cdot E$ which Demarcay [7] obtained by fusing exactly calculated amounts of the components. Although our data indicate the considerable stability of most esters to the action of titanium tetrachloride [1-6], there is information in the literature [8-15] about the splitting of ethers and esters in the presence of halides of aluminum and other metals which permits the assumption of an analogous reaction for some of the ester derivatives of titanium tetrachloride. Starting from the results of investigations of the decomposition of aluminum etherates [12-14], we assumed that the decomposition of the ester derivatives of titanium tetrachloride might occur when the esters which reacted with $TiCl_4$ consisted of strong acid residues and alcohol radicals with low electronegativity. This condition is satisfied by isopropyl formate, benzyl formate, and others [16], and the compound of $TiCl_4$ with the corresponding esters of trichloroacetic acid should tend to split even more easily.

According to ideas of polarization, among compounds of the types $TiCl_4 \cdot 2E$, $TiCl_4 \cdot E$, and $2TiCl_4 \cdot E$, most rapid decomposition would be expected in compounds of the last two types.

In the present work we give results of a study of the reaction of titanium tetrachloride with esters of the above structures. We also tested the results of Demarcay [7] on the compound $2TiCl_4 \cdot E$, whose existance we had not confirmed in the liquid phase, in order to explain its role in the decomposition of esters under the influence of titanium tetrachloride.

## EXPERIMENTAL

The esters, synthesized by the esterification reaction, after purification and drying [2-6] were fractionally distilled since the boiling point, refractive index, and density had not agreed with the literature data. Titanium tetrachloride was the same as in previous work [2-6]. As the solvent for obtaining the compounds we used carefully dried benzene. For washing the crystals which were obtained by mixing benzene solutions containing the calculated amounts of components, we used benzene and methylene chloride. The resulting washed and filtered compounds were placed in an apparatus which permitted carrying out operations without admitting moisture. The dry compounds were placed in a container with a stopcock and the air was pumped out. We used our method for determining titanium as $TiO_2$ (precipitated by ammonia) and we determined chloride by the Volhard method; these are recommended for analysis of similar compounds [17].

### Compounds $TiCl_4 \cdot E$ and $2TiCl_4 \cdot E$

As Table 1 shows, the compounds formed from solutions of titanium tetrachloride in esters of trichloroacetic acid have the equimolecular composition. They are unstable yellow crystals which dissociate into the starting compounds when they melt [6]. Due to their low melting points, we did not succeed in isolating the compounds $TiCl_4 \cdot$ n-$CCl_3COOC_4H_9$ and $TiCl_4 \cdot$ iso-$CCl_3COOC_5H_{11}$, even with cooling to −20°. Although the compounds $TiCl_4 \cdot CCl_3COOC_2H_5$ and $TiCl_4 \cdot CCl_3COO$ iso $C_4H_9$ easily dissociate into their components [6], decomposition of the esters was not found here. On the other hand, the compound $TiCl_4 \cdot$ iso-$CCl_3COOC_3H_7$ when weakly heated, splits energetically with the formation of products which indicate decomposition of the ester. The same result is found with the compound $TiCl_4 \cdot iso\text{-}HCOOC_3H_7$, but the decomposition in this case begins at a higher temperature.

To test the existence of compounds $2TiCl_4 \cdot E$ we studied the reaction of titanium tetrachloride with esters of benzoic acid, since, according to the data of Demarcay [7], the most stable compounds of this type were obtained by him by melting the calculated amounts of $TiCl_4$ with methyl and ethyl benzoate.

As Table 1 shows, when benzene solutions which contained equimolecular amounts of the components were mixed, the compounds formed had a 1:1 ratio.

TABLE 1

| Compound | Calculated (in wt. %) |  | Found (in weight %) |  |
|---|---|---|---|---|
|  | Ti | Cl | Ti | Cl |
| $TiCl_4 \cdot Cl_3CCOOC_2H_5$ . . . . . . | 12.56 | — | 12.47, 12.57 | — |
| $TiCl_4 \cdot iso\text{-}Cl_3CCOOC_3H_7$ . . . . | 12.12 | — | 12.66, 12.28 | — |
| $TiCl_4 \cdot iso\text{-}Cl_3CCOOC_4H_9$ . . . . | 11.70 | — | 11.78, 11.68 | — |
| $TiCl_4 \cdot n.\text{-}HCOOC_3H_7$ . . . . . . | 17.24 | 51.05 | 17.22, 17.29 | 50.87, 51.31 |
| $TiCl_4 \cdot C_6H_5COOC_2H_5$ . . . . . . | 14.09 | 41.72 | 14.14, 14.12 | 41.87, 41.82 |
| $TiCl_4 \cdot iso\text{-}C_6H_5COOC_4H_9$ . . . . | 13.02 | 38.54 | 13.36, 13.28 | 39.50, 39.24 |
| $TiCl_4 \cdot iso\text{-}C_6H_5COOC_5H_{11}$ . . . | 12.54 | 37.13 | 12.75, 12.69 | 37.65, 37.51 |
| $HCOOTiCl_3$ . . . . . . . . . . . | 24.03 | 53.37 | 24.10, 24.11 | 53.23, 53.30 |
| $Cl_3CCOOTiCl_3$ . . . . . . . . . | 15.12 | — | 15.21, 15.20 | — |

TABLE 2

| Compound | Titanium content (in weight %) |  |  |
|---|---|---|---|
|  | calculated | found |  |
|  |  | without washing | after washing with $C_6H_6$ |
| $2TiCl_4 \cdot CH_3COOC_2H_5$ . . . . . | 20.49 | 21.32, 21.22 | 17.42 |
| $2TiCl_4 \cdot C_6H_5COOC_2H_5$ . . . . . | 18.09 | 18.83, 18.88 | 14.33 |
| $2TiCl_4 \cdot n.\text{-}C_6H_5COOC_4H_9$ . . . | 17.18 | 17.99, 17.96 | 13.39 |
| $2TiCl_4 \cdot iso\text{-}C_6H_5COOC_5H_{11}$ . . . | 16.75 | 17.41, 17.51 | 12.78 |

The compound $TiCl_4 \cdot E$ crystallized from benzene solutions which contained $TiCl_4$ and the ester in the ratio 2:1. The same result was obtained using methylene chloride or carbon tetrachloride as solvents. Since we did not succeed in isolating the compound $2TiCl_4 \cdot E$ from solution, we tried to obtain it by adding a small amount of ester to an excess of titanium tetrachloride (0.2 g-mole of ester to 1 g-mole of $TiCl_4$). The results are shown in Table 2 which indicate that the crystals isolated from excess $TiCl_4$ have a composition close to a compound with ratio 2:1. However, even careful washing with benzene leads to decomposition of these compounds. The same result is obtained by washing with carbon tetrachloride and methylene chloride. Carbon tetrachloride and benzene do not react with titanium tetrachloride at room temperature [18, 19]; therefore the results allow us to conclude that the compound $2TiCl_4 \cdot E$, which can be considered to be formed by combination of $TiCl_4 \cdot E$ with $TiCl_4$, has slight stability, because of the high dipole moment of this compound [20].

### Decomposition of Compounds $TiCl_4 \cdot E$

To determine the direction of decomposition of the compounds $TiCl_4 \cdot iso\text{-}CCl_3COOC_3H_7$ and $TiCl_4 \cdot iso\text{-}HCOOC_3H_7$ we studied the volatile products which were evolved.

Decomposition of the compound $TiCl_4 \cdot iso\text{-}HCOOC_3H_7$ began at 60-70° and some excess of $TiCl_4$ favored this process. In the volatile products of the decomposition we noted besides $TiCl_4$ and $HCOOC_3H_7$, hydrogen chloride, carbon monoxide, and a liquid which burned with a blue flame and whose vapor condensed in a trap cooled by solid carbon dioxide. The vapors of such a liquid were also found in the decomposition of $TiCl_4 \cdot$ iso-$CCl_3COOC_3H_7$, which occurred more energetically and began at 30-35°. We did not find evolution of carbon monoxide in this case. The liquid formed in the decomposition conformed in its properties (characteristic odor, absence of reaction with bromine water) with isopropyl chloride. This was confirmed by the formation of isopropyl benzene by passing the vapors of the liquid through benzene which contained $AlCl_3$.

The results of the analysis of the nonvolatile products which remained after the decomposition, red-brown in the case of splitting of $TiCl_4 \cdot$ iso-$CCl_3COOC_3H_7$, and gray in the case of the decomposition of $TiCl_4 \cdot$ iso-$HCOOC_3H_7$, are given in the last two columns of Table 1.

The data permit us to conclude that the compounds $TiCl_4 \cdot E$ decompose by a reaction analogous [12-14] to that for aluminum trichloride: $TiCl_4 \cdot RCOOR' \rightarrow R'Cl + RCOOTiCl_3$, and in the case of formates there is partial further decomposition: $HCOOTiCl_3 \rightarrow HCl + CO + TiOCl_2$ and $TiOCl_2 \rightarrow TiCl_4 + TiO_2$.

We found that when $HCOOTiCl_3$ was heated, carbon monoxide, hydrogen chloride, $TiCl_4$, and $TiO_2$ were formed, which confirmed our assumption.

The decomposition of the compounds with ratio 1:1 formed from titanium tetrachloride with benzyl formate and especially with benzyl trichloroacetate occurred with warming and was so violent that it was not possible to isolate the compounds $TiCl_4 \cdot E$ though their formation was indicated by the appearance of a dark red color when equimolecular amounts of the components were mixed. The decomposition of these compounds was accompanied by violent evolution of hydrogen chloride and formation of a yellow tar insoluble in alcohol and ether, but easily soluble in chloroform and benzene. Decomposition of $TiCl_4 \cdot CH_3COOCH_2C_6H_5$ goes with evolution of hydrogen chloride and formation of the yellow tar, but the process in this case requires heating to 100-150° and goes less energetically.

Formation of a yellow tar was observed in the action of $SnCl_4$ on ethers and esters of benzyl alcohol, and also directly on benzyl chloride. The composition of the yellow product could conform to the formula $C_7H_6$ [21, 22]. The tar formed by this process [22] and formed in our experiments both have the formula $C_7H_6$. Some variation of the analytical data from the calculated value is explained by the difficulty in separating the product from benzene.

Analysis of the tar formed from $TiCl_4 \cdot HCOOCH_2C_6H_5$.

Found %: C 92.52, 92.57; H 7.00, 6.93. $C_7H_6$. Calculated %: C 93.29; H 6.71.

Analysis of the tar formed from $TiCl_4 \cdot CCl_3COOCH_2C_6H_5$.

Found %: C 92.67, 92.79; H 6.91, 7.05. $C_7H_6$. Calculated %: C 93.29; H 6.71.

Analysis of the tar formed from $TiCl_4 \cdot CH_3COOCH_2C_6H_5$.

Found %: C 92.97, 92.61; H 6.88, 7.04. $C_7H_6$. Calculated %: C 93.29; H 6.71.

Thus the results confirm the assumption of the decomposition of the compounds $TiCl_4 \cdot E$ with formation of the product $RCOOTiCl_3$ and alkyl halides, and in the case of separation of benzyl chloride, the process is complicated by its condensation with the formation of the hydrocarbon $C_7H_6$.

The finding of hastening of the decomposition of these compounds by addition of excess $TiCl_4$ can be explained by partial formation of the unstable compound $2TiCl_4 \cdot E$.

## SUMMARY

1. We have established that titanium tetrachloride gives compounds with a 1:1 ratio with esters of trichloroacetic or benzoic acids.

2. We have confirmed the existence in the solid phase of the compounds $2TiCl_4 \cdot E$ and shown the instability of the bond of the second molecule of $TiCl_4$ with $TiCl_4 \cdot E$.

3. We have shown that some compounds $TiCl_4 \cdot E$ can decompose in the same way as etherates of aluminum trichloride and explained the conditions of the decomposition.

## LITERATURE CITED

[1] O. A. Osipov and V. Ia. Suchkov, J. Gen. Chem. 22, 1132 (1952).*

[2] Iu. A. Lysenko and O. A. Osipov, J. Gen. Chem. 24, 53 (1954).*

[3] O. A. Osipov, Iu. A. Lysenko and E. K. Akopov, J. Gen. Chem. 25, 249 (1955).*

[4] O. A. Osipov and E. E. Kravtsov, J. Gen. Chem. Supp. 1, 216 (1953).

[5] Iu. A. Lysenko, J. Gen. Chem. 26, 2963 (1956).*

[6] Iu. A. Lysenko, J. Gen. Chem. 26, 3273 (1956).*

[7] M. E. Demarcay, Bull. Soc. Chim. 20, 127 (1873).

[8] G. A. Stadnikov and L. I. Kashtanov, J. Russ. Phys. Chem. Soc. 60, 1117 (1928).

[9] L. I. Kashtanov, J. Gen. Chem. 2, 315 (1932).

[10] L. I. Kashtanov, J. Gen. Chem. 3, 223 (1933).

[11] L. I. Kashtanov, J. Gen. Chem. 4, 1204 (1934).

[12] D. N. Kursanov and R. R. Zel'vin, J. Gen. Chem. 9, 2173 (1939).

[13] V. D. Geoshvili, Symp. Tr. Gruzinsk. Politekh. Inst. 17, 389 (1948).

[14] A. F. Dobrianskii and Iu. I. Kornilov, J. Gen. Chem. Supp. 1, 320 (1953).

[15] B. V. Tronov and A. M. Petrova, J. Gen. Chem. 23, 1019 (1953).*

[16] H. C. Brown, J. Am. Chem. Soc. 61, 1483 (1939).

[17] O. C. Dermer and W. C. Fernelius, Z. allg. anorg. Ch. 221, 83 (1934).

[18] G. P. Luchinskii, Tetravalent Titanium, Oborongiz, 1939.**

[19] M. N. Cullinane, S. J. Chard and D. M. Leyshon, J. Chem. Soc. 1952, 4106.

[20] O. A. Osipov, J. Gen. Chem. 26, 322 (1956).*

[21] N. S. Tsonev, J. Russ. Phys. Chem. Soc. 48, 550 (1916).

[22] Ia. L. Gol'dfarb and L. M. Smorgonskii, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1, 65 (1936).

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# TERNARY CONJUGATE SYSTEM OF LITHIUM AND SODIUM BUTYRATES AND NITRATES

N. M. Tsindrik and N. M. Sokolov

The present work was undertaken with the purpose of showing the direction of exchange reaction between fused sodium and lithium butyrates and nitrates. It is interesting to compare this system with the previously studied systems of lithium and sodium formates, acetates, propionates and nitrates of the same metals.

## EXPERIMENTAL

The liquidus surface of the system was studied by a visual-polythermal method. A nichrome-constantan thermocouple and a millivoltmeter were used to measure the temperatures at which first crystals appeared. Addition of excess butyric acid to a solution of chemically pure carbonates, followed by evaporation, produced lithium and sodium butyrates [1]. The dry salts obtained were then purified by recrystallization from butanol.

The melting points of the components in our systems were: $LiNO_3$ 256°, $NaNO_3$ 308°, $C_3H_7COOLi$ 329°, $C_3H_7COONa$ 330°. A polymorphic transition of sodium nitrate is known at 275°. For sodium butyrate polymorphic transitions were determined at 117, 232, 252, and 316° [2].

### Side Faces (Table 1, Fig. 1)

1. $LiNO_3-NaNO_3$ system has been investigated by many authors. The components form a eutectic mixture. According to our data the eutectic point is at 198° and 45% sodium nitrate.

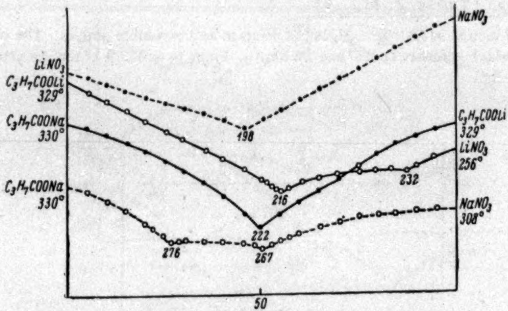

Fig. 1. Melting point curves of binary systems.

2. $LiNO_3-C_3H_7COOLi$ system was studied for the first time. The three branches of the melting curve intersect at 232° and 15%, 216° and 45% of $C_3H_7COOLi$. The probable composition of the compound is $7LiNO_3 \cdot C_3H_7COOLi$.

TABLE 1

Binary Systems

| $LiNO_3$—$NaNO_3$ | | $LiNO_3$—$C_3H_7COOLi$ | | $C_3H_7COOLi$—$C_3H_7COONa$ | | $C_3H_7COONa$—$NaNO_3$ | |
|---|---|---|---|---|---|---|---|
| Mole % of $NaNO_3$ | Temp. | Mole % of $C_3H_7COOLi$ | Temp. | Mole % of $C_3H_7COONa$ | Temp. | Mole % of $NaNO_3$ | Temp. |
| 0 | 256° | 0 | 256° | 0 | 329° | 0 | 330° |
| 5 | 250 | 5 | 248 | 5 | 326 | 5 | 325 |
| 10 | 242 | 10 | 242 | 10 | 318 | 10 | 316 |
| 15 | 236 | 12.5 | 238 | 15 | 308 | 15 | 306 |
| 20 | 230 | 15 | 232 | 20 | 298 | 20 | 294 |
| 25 | 224 | 17.5 | 232 | 25 | 285 | 22.5 | 286 |
| 30 | 216 | 20 | 232 | 30 | 273 | 25 | 280 |
| 35 | 210 | 25 | 230 | 35 | 260 | 26.5 | 276 |
| 40 | 204 | 30 | 230 | 40 | 248 | 27.5 | 276 |
| 45 | 198 | 35 | 226 | 45 | 234 | 30 | 276 |
| 50 | 208 | 40 | 224 | 50 | 222 | 35 | 274 |
| 55 | 219 | 42.5 | 220 | 55 | 240 | 40 | 274 |
| 60 | 230 | 45 | 216 | 60 | 254 | 45 | 270 |
| 65 | 240 | 50 | 228 | 65 | 270 | 47.5 | 268 |
| 70 | 250 | 55 | 238 | 70 | 280 | 50 | 267 |
| 75 | 260 | 60 | 248 | 75 | 292 | 52.5 | 274 |
| 80 | 270 | 65 | 258 | 80 | 302 | 55 | 278 |
| 90 | 290 | 70 | 268 | 85 | 312 | 60 | 284 |
| 95 | 300 | 75 | 278 | 90 | 320 | 65 | 290 |
| 100 | 308 | 80 | 288 | 95 | 327 | 70 | 292 |
| | | 85 | 298 | 100 | 330 | 75 | 296 |
| | | 90 | 308 | | | 80 | 300 |
| | | 100 | 329 | | | 90 | 304 |
| | | | | | | 100 | 308 |

3. $C_3H_7COOLi-C_3H_7COONa$ system was also studied for the first time. The eutectic point is at 222° and 50% $C_3H_7COONa$.

4. $C_3H_7COONa-NaNO_3$ system was previously described [3]. The three branches of the melting curve have eutectic points at 276° and 28%, 267° and 50% sodium nitrate. Probable composition of the compound is $3C_3H_7COONa \cdot NaNO_3$.

## Diagonal Sections (Table 2, Fig. 2)

Stable diagonal section of $NaNO_3-C_3H_7COOLi$ points to an irreversible process. The melting curve consists of two branches which intersect at 298° and 9% $NaNO_3$. From 10 to 97.5% of sodium nitrate phase-separation is observed.

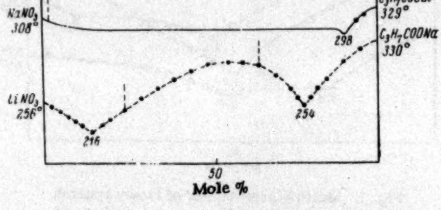

Fig. 2. Diagonal sections of ternary conjugate systems.

Unstable diagonal section $LiNO_3-C_3H_7COONa$ is made up of three branches ($LiNO_3$, $C_3H_7COONa$, and a branch of exchange product) which intersect in two places: 216° and 16%, 254° and 78% $C_3H_7COONa$. Phase-separation takes place in this section from 25 to 79% of $C_3H_7COONa$.

## Internal Sections

We investigated 25 internal sections to find the surfaces of crystallization fields in the system; the directions of these sections are shown in Fig. 3, and their characteristics given in Figs. 4 and 5.

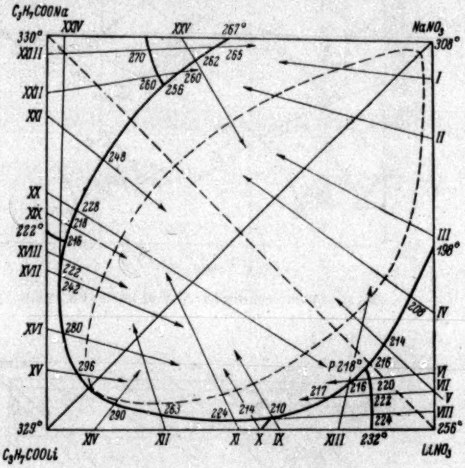
C₃H₇COONa
NaNO₃
C₃H₇COOLi
LiNO₃
330°
308°
329°
256°
222°
198°
267°
232°
P 218°
XXIV
XXV
XXIII
XXII
XXI
XX
XIX
XVIII
XVII
XVI
XV
XIV
XII
XI
X
IX
XIII
I
II
III
IV
VI
VII
V
VIII
270
262
265
260
260
256
248
228
218
216
222
242
280
296
290
263
224
214
210
208
214
216
217
216
220
222
224

Fig. 3. Directions of internal sections.

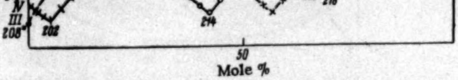

Fig. 4. Characteristics I-VIII of internal sections.

Using the results of our investigation of binary systems and internal sections, we projected the three-dimensional crystallization surfaces onto a square composition diagram (Fig. 6). The surface of the liquidus system consists of 6 fields. $NaNO_3$ field occupies 77.96%; $LiNO_3$, 5.37%; $C_3H_7COONa$, 9.05%; $C_3H_7COOLi$, 4.19%; $7LiNO_3 \cdot C_3H_7COOLi$, 2.21%, and $3C_3H_7COONa \cdot NaNO_3$, 1.22% of the total surface. Phase separation is located along the

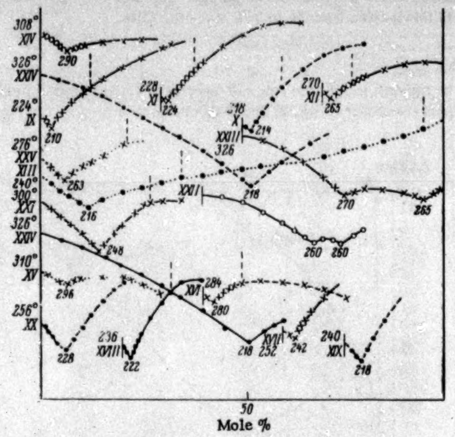

Fig. 5. Characteristics IX-XXV of internal sections.

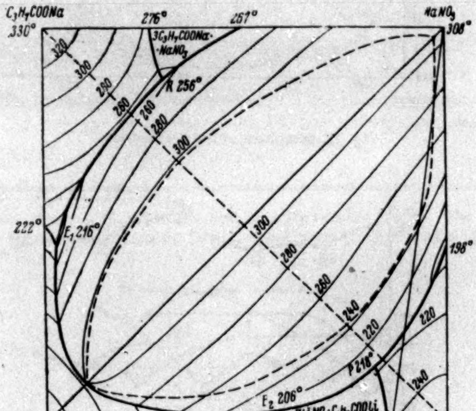
C₃H₇COONa
330°
276°
261°
NaNO₃
308°
3C₃H₇COONa·NaNO₃
R 256°
320
300
290
280
260
280
300
222°
E₁ 216°
300
280
260
240
220
220
198°
P 218°
240
E₂ 206°
7LiNO₃·C₃H₇COOLi
329°
C₃H₇COOLi
216°
232°
256°
LiNO₃

Fig. 6. Projection of a conjugate system diagram onto a composition square.

stable diagonal section in the form of a lens on the sodium nitrate field and occupies 66% of its area or 51.5% of the total liquidus surface area. The ternary eutectic curves intersect in two eutectic points, and in two other invariant points, which are of Type 1 and Type 2, respectively (at which one and two, respectively, of the three invariants lines fall to the invariant point and the others rise). Temperatures and compositions are listed in Table 3.

**TABLE 2**

**Diagonal Sections**

| $C_3H_7COOLi-NaNO_3$ | | $C_3H_7COONa-LiNO_3$ | |
|---|---|---|---|
| Mole % of $C_3H_7COOLi$ | Temperature | Mole % of $LiNO_3$ | Temperature |
| 0 | 308° | 0 | 330° |
| 1 | 304 | 5 | 324 |
| 2.5 | 300 | 10 | 304 |
| 5 | 300 | 15 | 284 |
| 25 | 300 | 17.5 | 272 |
| 50 | 300 | 20 | 260 |
| 90 | 300 | 21 | 254 |
| 91 | 298 | 22.5 | 260 |
| 92.5 | 302 | 25 | 272 |
| 94 | 308 | 27.5 | 282 |
| 96 | 318 | 30 | 292 |
| 98 | 324 | 35 | 300 |
| 100 | 329 | 50 | 300 |
| | | 55 | 296 |
| | | 60 | 284 |
| | | 70 | 258 |
| | | 80 | 230 |
| | | 82.5 | 222 |
| | | 85 | 216 |
| | | 87.5 | 224 |
| | | 90 | 234 |
| | | 95 | 246 |
| | | 100 | 256 |

**TABLE 3**

| Point | Type of point | Temp. | Composition (in mole %) | | | |
|---|---|---|---|---|---|---|
| | | | $LiNO_3$ | $NaNO_3$ | $C_3H_7COONa$ | $C_3H_7COOLi$ |
| $E_1$ | Eutectic | 216° | — | 4 | 44 | 52 |
| $E_2$ | Eutectic | 206 | 57.5 | 2.5 | 40 | — |
| $P$ | Type 1 | 218 | 67.5 | 14 | — | 18.5 |
| $R$ | Type 2 | 256 | — | 30 | 58 | 12 |

Figure 7 shows the location of invariant points and ternary eutectic lines projected on the $C_3H_7COOLi-LiNO_3$ side.

The stable diagonal section and the one leading from the supposed terminal of compound $7LiNO_3 \cdot C_3H_7COOLi$ to the top of $NaNO_3$ separate the square surface of the system into three-phase triangles: $NaNO_3-C_3H_7COONa-C_3H_7COOLi$, $NaNO_3-C_3H_7COOLi-$compound $7LiNO_3 \cdot C_3H_7COOLi$, $NaNO_3-$compound $7LiNO_3 \cdot C_3H_7COOLi-LiNO_3$.

We have previously investigated the conjugate formate, acetate, propionate and nitrate systems of lithium and sodium [4]. All these systems are of the diagonal type. Sodium nitrate and lithium salts of fatty acids form stable salt-pairs.

When the same geometrical elements of various systems [5] (stable diagonals and stable triangles) are compared, one observes that with increase in the number of carbon atoms in the radical the degree of equilibrium displacement increases.

## SUMMARY

1. The liquidus surface of a ternary conjugate system of lithium and sodium butyrates and nitrates was studied for the first time.

2. The data on two binary systems: $LiNO_3-C_3H_7COOLi$ and $C_3H_7COOLi-C_3H_7COONa$ are reported for the first time.

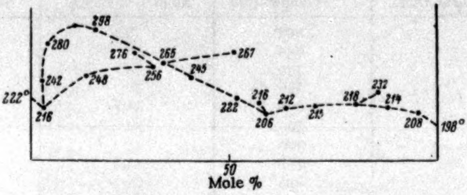

Fig. 7. The eutectic line projected on $C_3H_7COOLi-LiNO_3$ side.

3. The dependence of chemical equilibrium shift on the number of carbon atoms in the fatty acid radical was determined for a series of systems; the systems were those of formates, acetates, propionates, and butyrates and nitrates of lithium and sodium.

## LITERATURE CITED

[1] N. M. Sokolov, J. Gen. Chem. 24, 1581 (1954).*

[2] N. M. Sokolov, Theses of the Smolensk Med. Inst. Scientific Conference (1956).**

[3] N. M. Sokolov, J. Gen. Chem. 24, 1158 (1954).*

[4] N. M. Tsindrik, N. M. Sokolov, Theses of the Smolensk Med. Inst. Science Sessions (1954).**

[5] A. P. Palkin, ISFKhA AN SSSR, 17, 228 (1949).

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Smolensk State Medical Institute

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* Original Russian pagination. See C. B. Translation.

** In Russian.

# NEW REGULARITIES IN THE PHYSICOCHEMICAL PROPERTIES OF HYDROCARBONS. II*

V. M. Tatevskii and V. A. Benderskii

In preceeding papers [1-3] we have shown that a series of hydrocarbon properties (those properties which as a rule contain capacity factors, for example: molar volume V, molar refraction R, heat of formation from atoms $\Delta H_{(at.)}$ or elements $\Delta H_{(el.)}$, heat of combustion $\Delta H_{(comb.)}$, heat of vaporization L, logarithm of the vapor pressure log p et al.), when converted to molar units are a linear function of the number (n) of carbon atoms in the hydrocarbon molecule. According to the theoretical ideas previously developed by us [1, 3], this linearity should be observed for specific hydrocarbon groups with the same structure in the branched sections of the hydrocarbon chain.

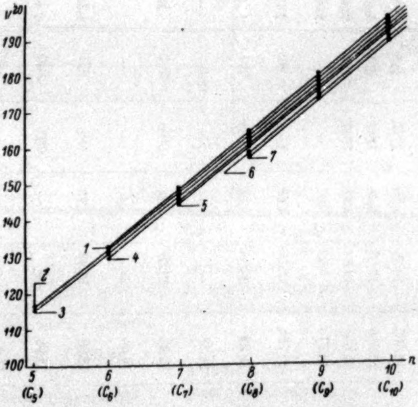

Fig. 1. Molar volumes $V^{20}$ as a function of the number of carbon atoms (n) in alkane molecules of various groups.
1) 2,2-Dimethylalkanes; 2) 2-methylalkanes; 3) n-alkanes; 4) 3-methylalkanes; 5) 3,3-dimethylalkanes; 6) 3,4-dimethylalkanes; 7) 2,3,3-trimethylalkanes.

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*For communication I see [3].

Values of Constants $\alpha^{(m)}$ and $\beta^{(m)}$ for Various Physicochemical Properties of Some Homologous Alkane Groups

| Alkane group | $V^{(20)}$ ml/mole | | $\Delta H_{(el.)}$ (kcal/mole) | | $L^{\circ}_{vap.}$ (kcal/mole), t = 130-170° | | Log $P_{60}$ (mm of Hg) | | $d_4^{(20)}$ | | | $t_b$ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $\alpha$ | $\beta$ | $\alpha$ | $\beta$ | $\alpha$ | $\beta$ | $\alpha$ | $\beta$ | $A$ | $B$ | $n_0$ | $t_0$ | $B$ | $n_0$ |
| n-Alkanes | 34.04 | 16.108 | —10.25 | —4.95 | 1750 | 857 | 5.322 | —0.428 | 0.8496 | —1.2875 | 0.7647 | 782.18 | 16402 | 17.98 |
| 2-Methylalkanes | 37.02 | 15.838 | 12.58 | 4.86 | 1843 | 811 | 5.401 | —0.421 | 0.8526 | —1.3795 | 0.92 | 822.93 | 18724 | 18.55 |
| 3-Methylalkanes | 33.31 | 16.069 | —11.57 | —4.91 | 2041 | 784 | 5.307 | —0.412 | 0.8682 | —1.5915 | 1.8 | 934.97 | 25591 | 23.56 |
| 3-Ethylalkanes | 29.76 | 16.270 | — 9.92 | 5.06 | — | — | 5.084 | —0.383 | | | | 2683.02 | 265104 | 95.38 |
| 2,2-Dimethyl-alkanes | 37.40 | 15.888 | 16.36 | 4.68 | 1516 | 789 | 5.452 | —0.406 | 0.8548 | —1.4224 | 0.9172 | 983.95 | 28701 | 24.72 |
| 2,3-Dimethyl-alkanes | 30.63 | 16.22 | 23.05 | 3.51 | 1805 | 791 | 5.184 | —0.389 | 0.8503 | —1.2410 | 1.0 | 1246.52 | 50390 | 36.56 |
| 2,4-Dimethyl-alkanes | 31.90 | 16.38 | — | — | — | — | — | — | | | | | | |
| 3,3-Dimethyl-alkanes | 32.84 | 15.98 | 17.09 | 4.44 | 1604 | 792 | 5.201 | —0.383 | | | | 1603.43 | 87344 | 50.56 |
| 3,4-Dimethyl-alkanes | 31.41 | 15.95 | — | — | — | — | | | | | | | | |
| 2,(n-1)Dimethyl-alkanes | 37.00 | 15.98 | 13.93 | 4.91 | 581 | 921 | 5.569 | —0.425 | | | | 818.62 | 18380 | 17.90 |
| 2,2,(n-1)-Tri-methylalkanes | 34.99 | 15.98 | — | — | 785 | 840 | 6.879 | —0.562 | | | | | | |
| 2,2,3,3-Tetra-methylalkanes | 20.00 | 16.61 | — | — | — | — | | | | | | | | |

In the present work it is shown that theoretical predictions were actually borne out by experimental data covering various physicochemical properties of paraffin hydrocarbons (alkanes).

According to the theory [3], all the alkanes can be separated into groups on the basis of identical structure in branched fragments of hydrocarbon chains. Examples of such groups are listed in the Table. Then, for each (for example n-th) alkane group some physicochemical dimension P (from among the ones listed above) should be a linear function of the number of carbon atoms (n) in the alkane molecule of that group,

$$P_n^{(m)} = 2P_{12} - 3P_{22} + \Delta^{(m)} + P_{22} \cdot n, \tag{1}$$

with a constant coefficient $P_{22}$.

Equation (1) can be rewritten in a shorter form,

$$P_{(n)}^{(m)} = \alpha^{(m)} + \beta \cdot n, \tag{2}$$

where: $\alpha^{(m)}$ = constant for a given group, $\beta$ = constant for all the groups. In Figs. 1-4 we have shown to what degree is linear dependence (1), (2) of different physicochemical properties fulfilled in each alkane group. It is evident from these figures that the agreement between theory and experiments is completely satisfactory. The values of group constants $\alpha^{(m)}$ were calculated from experimental data and are listed in the Table; in going from group to group we can see a change not only in $\alpha^{(m)}$ (as theoretically expected) but also an insignificant one in $\beta$, although theoretically it should remain constant for all the groups. However, these variations in $\beta$ are negligible and its value is very close to constant (as the theory would require).

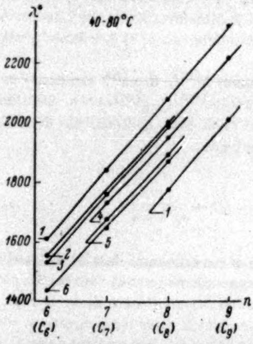

Fig. 2. $\lambda^0 = \frac{L^0}{4.575}$ as a function of the number of carbon atoms in alkane molecules of various groups.

1) n-Alkanes; 2) 3-methylalkanes; 3) 2-methylalkanes; 4) 2,3-dimethylalkanes; 5) 3-ethylalkanes; 6) 2,2-dimethylalkanes; 7) 2,2(n-1)-trimethylalkanes.

Value of $\lambda^0$ are in the interval 40-80°.

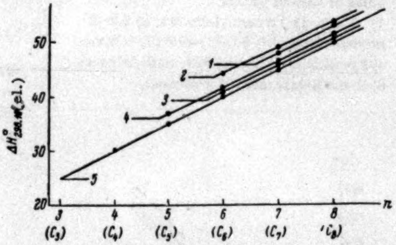

Fig. 3. $\Delta H^0_{(el.)}$ gas at T = 298.16°K as a function of the number (n) of carbon atoms in alkane molecules of various groups.

1) 2,(n-1)-Dimethylalkanes; 2) 2,2-dimethylalkanes; 3) 3-methylalkanes; 4) 2-methylalkanes; 5) n-alkanes.

For such factors as density and boiling point of hydrocarbons in each group we derived [3] equations of the type:

$$d_n^{(m)} = \frac{a^{(m)} + b \cdot n}{g^{(m)} + h \cdot n} \tag{3}$$

For calculations it is convenient to change it to this form:

$$d_n^{(m)} = A^{(m)} + \frac{B}{n_0^{(m)} + n}, \tag{4}$$

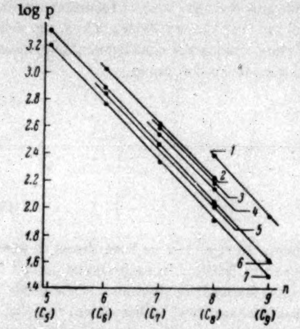

Fig. 4. The logarithm of vapor pressure (at constant temperature 60°) as a function of the number of carbon atoms in alkane molecules of various groups.
1) 2,2,(n-1)-Trimethylalkanes; 2) 2,2-dimethylalkanes; 3) 2,(n-1)-dimethylalkanes; 4) 3,3-dimethylalkanes; 5) 3-methylalkanes; 6) 2-methylalkanes; 7) n-alkanes.

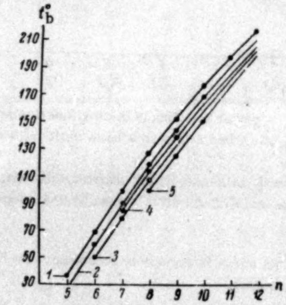

Fig. 6. Boiling point t as a function of the number of carbon atoms (n) in alkane molecules of various groups.
1) n-Alkanes; 2) 2-methylalkanes; 3) 2,2-dimethylalkanes; 4) 3,3-dimethylalkanes; 5) 2,2,(n-1)-trimethylalkanes.

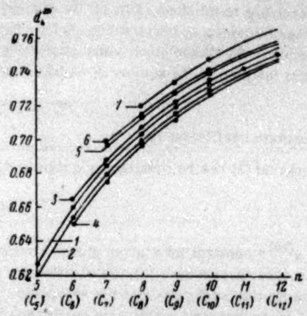

Fig. 5. Density $d_4^{20}$ as a function of the number of carbon atoms in alkane molecules of various groups.
1) n-Alkanes; 2) 2-methylalkanes; 3) 3-methylalkanes; 4) 2,2-dimethylalkanes; 5) 2,3-dimethylalkanes; 6) 6-ethylalkanes; 7) 3,4-dimethylalkanes.

where the new constant $A^{(m)}$, B, $n_0^{(m)}$ can easily be expressed through constants $a^{(m)}$, b, $g^{(m)}$, and n. Similarly, for the boiling point of m-th group hydrocarbons the following equation can be derived:

$$t_n^{(m)} = t_0^{(m)} + \frac{B}{n_0^{(m)} + n} \tag{5}$$

Comparisons of experimental data on $d_4^{20}$ and $t_b$ (at 760 mm) (for some alkane groups) with results calculated using Formulas (4) and (5) are shown in Figs. 5 and 6. The constants which enter these equations were calculated from experimental data and are listed in the Table.

It is evident from Fig. 4 that Equations (4) and (5) for $d_4^{20}$ and $t_b$ give a satisfactory description of regularities in each alkane group.

The above described regularities can readily be used to calculate physicochemical properties of as yet unstudied hydrocarbons of a given group, if corresponding experimental data is available for other hydrocarbons of the same group; this undoubtedly is of substantial interest in a number of practical cases. For example, we can use the constants from the Table in Formulas (2), (4) and (5) to calculate physicochemical properties of higher hydrocarbons belonging to groups listed in the same Table.

## LITERATURE CITED

[1] V. M. Tatevskii, Chemical Structure of Hydrocarbons and Regularities in Their Physicochemical Properties, Izd. MGU (1953).*

[2] V. M. Tatevskii, Proc. Acad. Sci. USSR 109, 131 (1956).**

[3] V. M. Tatevskii, Proc. Acad. Sci. USSR 113, 836 (1957).**

[4] Ref. Physicochemical Properties of Hydrocarbons, M.D. Tailcheeva ed., Nos. 3, 4, and 5, State Thermotech. Press (1949-1954).*

[5] F. D. Rossini, Selected Values of Properties of Hydrocarbons, Washington (1953).

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*In Russian.

**Original Russian pagination. See C. B. Translation.

# REACTIONS OF POLYHALOGEN COMPOUNDS WITH ALCOHOLS

N. S. Vasileiskaya

Reactions of carbon tetrachloride with methyl [1] and ethyl [2] alcohols were studied in the previously published papers. These reactions proceed on heating to 200° according to the scheme: $CCl_4 + ROH \rightarrow CHCl_3 + HCl + RC(O)H$. After this, the secondary processes of formation of alkyl chloride and ethers take place. The reaction of carbon tetrachloride with alcohols, with formation of hydrogen chloride proceeds even at lower temperatures under irradiation with ultraviolet light [1], $\gamma$-rays [3] and under the influence of an initiator [4].

It appeared interesting to us to determine whether or not these regularities extend to other alcohols and other polyhalogen compounds. With this purpose in mind we studied the thermal reactions of carbon tetrachloride with 1-butanol, 2-butanol, and, on the other hand, the reaction of pentachloroethane and tetrachloroethanes (symmetric and unsymmetric) with methanol.

The reactions of 1-butanol with carbon tetrachloride proceed at a higher temperature (230°) than that with methanol, forming chloroform, hydrogen chloride, water and butyl chloride. However, butyraldehyde could not be detected among the reaction products while butyl butyrate was actually found. Formation of the latter substance may be explained by an ester condensation of butyraldehyde formed in the first stage of the reaction: $2C_3H_7CHO \rightarrow C_3H_7COOC_4H_9$.

Reaction of 2-butanol with carbon tetrachloride proceeds at 210-220° with formation of the expected products: chloroform, hydrogen chloride, methyl ethyl ketones, water and secondary butyl chloride. However, in addition to these substances there were found butylene and a compound with composition $C_5H_8Cl_4$. The structure of the latter was not established. Possibly it was a product of addition of carbon tetrachloride to butylene. The formation of olefins had been noted by us earlier in the reaction of cyclohexanol with carbon tetrachloride. A large amount of cyclohexene was found along with the other products [5].

Thus it was shown that other primary and secondary alcohols react with carbon tetrachloride analogously to the reaction of methyl alcohol.

Then we examined the reactions of pentachloroethane and symmetric and unsymmetric tetrachloroethanes with methyl alcohol.

The radical decomposition of pentachloroethane takes place during irradiation with ultraviolet light and yields hydrogen chloride with dimerization of the resulting radicals [6]. In addition to this there are observed reactions of chlorination of both the pentachloroethane and the resulting derivatives of butane. Hexachloroethane, octachlorobutane, nonachlorobutane and decachlorobutane were isolated.

Hydrogen chlroride, formaldehyde, methyl chloride, water, 1,1,2,2-tetrachloroethane and trichloroethylene were isolated after the thermal reaction of pentachloroethane with methanol (210-220°). On the basis of the data obtained one may consider that the process proceeds according to the following equation: $CHCl_2-CCl_3 + CH_3OH \rightarrow CHCl_2-CHCl_2 + CH_2O + HCl$. Formation of trichloroethylene may occur either through cleavage of hydrogen chloride from tetrachloroethane or through the decomposition of the primary radical with evolution of chlorine:

$$CHCl_2-CHCl_2 \longrightarrow CHCl=CCl_2 + HCl$$
$$CHCl_2-CCl_2\cdot \longrightarrow CHCl=CCl_2 + Cl\cdot$$

The last reaction is analogous to the cleavage of pentachloroethyl radical [7]. The formation of $CHCl_2-CCl_2^{\cdot}$ may be regarded as the primary process in the cleavage of chlorine from the $CCl_3$ group. Thus, the first stage of the process would be the same for $CCl_4$, $C_2Cl_6$ and $C_2HCl_5$.

The difference between the reactions of hexachloroethane and pentachloroethane with methanol consists of the fact that the $C_2Cl_5^{\cdot}$ radical is incapable of cleavage of a hydrogen atom from the alcohol and suffers a total decomposition with evolution of chlorine and formation of perchloroethylene [2]. The $C_2HCl_4^{\cdot}$ radical is able, one one hand, to cleave a hydrogen from the alcohol just like $CCl_3^{\cdot}$ radical, and, on the other hand, it can lose chlorine just like $C_2Cl_5^{\cdot}$ radical.

The correctness of the previously made supposition about the absence of the reaction of hydrogen cleavage from the alcohol by the $C_2Cl_5^{\cdot}$ radical has been confirmed by the data in this investigation. If such a reaction did take place, the resulting $C_2HCl_5$ would have reacted further and should have formed $C_2HCl_4$ and trichloroethylene. Thus, the reaction with pentachloroethane proceeds by the following scheme:

$$C_2HCl_5 \longrightarrow CHCl_2-CCl_2\cdot + Cl\cdot$$
$$Cl\cdot + CH_3OH \longrightarrow HCl + \cdot CH_2OH \text{ or}$$
$$CHCl_2CCl_2\cdot + CH_3OH \longrightarrow CHCl_2-CHCl_2 + \cdot CH_2OH$$

In this scheme we presuppose a dissociation at the C–Cl bond in the trichloromethyl group. For a confirmation of this supposition we studied the reaction of methanol with symmetric and unsymmetric tetrachloroethane. This reaction is interesting also from the viewpoint that the symmetric $C_2H_2Cl_4$ is a reaction product of methanol and pentachloroethane.

However, the data obtained by us did not permit us to make any definite conclusions. 1,1,2,2-Tetrachloroethane reacts with methanol at 220-230° with formation of trichloroethylene, water, hydrogen chloride and methyl chloride. Only traces of formaldehyde were detected. This shows that the cleavage of chlorine almost does not occur and the reaction, in the main, proceeds by the scheme:

$$CHCl_2-CHCl_2 \longrightarrow HCl + CHCl=CCl_2$$
$$CH_3OH + HCl \longrightarrow CH_3Cl + H_2O$$

1,1,1,2-Tetrachloroethane reacts with methanol at 215-220°. In this case water, hydrogen chloride and methyl chloride are formed, along with considerable amounts of tar. Only traces of formaldehyde were detected. Trichloroethylene could not be found. However, the tar containing but 23% of chlorine could form in copolymerization of formaldehyde with halogen compounds.

## EXPERIMENTAL

The reaction mixture was sealed into tubes of thick-walled heat resistant glass with length of 60-70 cm and diameter of 12-15 mm. Heating of the tubes was done in tube furnaces until the volume of the resulting aqueous layer ceased to change. The tubes were chilled with a mixture of solid carbon dioxide and toluene prior to being opened. A gas, which was collected in chilled absorption flasks, was evolved in some cases on slow heating of the tubes to room temperature. In experiments with methanol the gas was first passed through water (for absorption of hydrogen chloride and formaldehyde), then through alcoholic ammonia. After cessation of gas evolution the tube with alcoholic ammonia was sealed and heated on a water bath for completion of the formation of the amine salt from methyl chloride and ammonia. Then the mixture was diluted with water and was analyzed for chlorine, from the amount of which there was calculated the yield of methyl chloride. Water through which the gas had been passed did not contain hydrogen chloride or formaldehyde in all the experiments run. The upper aqueous layer was separated after the elimination of gases from the reaction tube. The nonaqueous part was washed with water. Then each layer was analyzed separately. Formaldehyde was determined in the form of dimedone derivative in the aqueous reaction layer as well as in the wash water and after the hydrolysis of the resulting methylal. It was not possible to isolate a sufficient amount of completely pure products in all cases by distillation through a fractionating column (25 theoretical plates) even after repeating the operations several times. Owing to this the elemental analysis in some instances deviated from the theoretical value by 1-2%.

A spectroscopic analysis of some fractions was made following the experiments with 1-butanol and 2-butanol, in addition to the chemical analysis. The spectra of the solutions under study were recorded in the interval from 15 to 4$\mu$ on a double beam IKS-2 spectrometer with potassium chloride prism. The thickness of the absorbing layer was 0.1 mm. The identification of the absorption lines which belong to the substance under study was done by comparison of its spectrum with the spectrum of authentically pure substance recorded on the same machine.

1-Butanol–Carbon Tetrachloride. Sixteen g (0.217 mole) of butanol, 16.0 g (0.104 mole) of carbon tetrachloride were heated 20-30 hours at 230°. The evolved gas (0.200 g) was passed into bromine water for determination of butylene. The bromine water was not decolorized. The weight of the aqueous layer was 1.7 g, and that of nonaqueous part was 30.0 g. The aqueous layer and the water from washing the nonaqueous layer contained 0.062 g of hydrogen chloride which was determined by titration. The nonaqueous layer, after washing, weighed 5.7 g less (owing to removal of butanol). After drying with sodium sulfate, the nonaqueous part was distilled through a column with 25 theoretical plate efficiency. A mixture from six reaction tubes was used for this distillation. The first fraction at 60-72° (71.15 g) was examined spectroscopically. Chloroform ($\lambda$, 8.2 and 10.9 $\mu$) and primary butyl chloride ($\lambda$ 7.3, 8.5 $\mu$) and others) were found in it by the method of spectral coincidence. After two redistillations through the fractionating column, a chloroform fraction (61.3-63.0°), with $d^0_0$ 1.5025, $n^{20}D$ 1.440 (qualitative test with resorcinol for chloroform was positive) was isolated from the first fraction. The amount of chloroform determined by heating with aniline, alkali and methanol [8] was 4.28 g calculated for the contents of one reaction tube. The residue after the distillation of the first fraction was distilled at 25 mm vacuum. There was collected the second fraction at 60-75° (1.9 g), $d^0_0$ 0.8937, $n^{20}D$ 1.4113, which consisted of butyl ester of butyric acid (this fraction had the characteristic odor of an ester). The content of butyl butyrate (as determined by saponification of 0.5 N aqueous alcoholic alkali) was 97%. The molecular weight was 138 (calculated 144). The absence of butyraldehyde in the reaction products was proved spectroscopically (by absence of the absorption line of butyraldehyde in the absorption spectra) and by a negative reaction with semicarbazide and 2,4-dinitrophenylhydrazine.

2-Butanol–Carbon Tetrachloride. Sixteen g (0.217 mole) of 2-butanol and 16.0 g (0.104 mole) of carbon tetrachloride were heated 16-20 hours at 210-220°. The butylene generated in the reaction mixture (6.0 g) was transformed into dibromobutane (b.p. 160°, $d^0_0$ 1.8256) by passage into bromine water. The aqueous layer (3.6 ml) and the wash water contained 0.3 g of hydrogen chloride. Four tenths of a gram of methyl ethyl ketone was found in the wash water; 2,4-dinitrophenylhydrazone, m.p. 109° (no depression in mixed melting with authentic sample). The quantitative determination was made by the reaction with hydroxylamine hydrochloride. The nonaqueous part was distilled through the column after washing and drying with sodium sulfate. The mixture from six reaction tubes (114.2 g) was taken for the distillation. There was isolated the following fractions: 1st 58.5-67.0°, 8.6 g; 2nd 67.0-69.0°, 27.0 g; 3rd 69.0-73.0°, 24.1 g; 4th 74-78°, 3.2 g; residue 25.7 g. Three and three tenths grams of butylene was isolated in addition during the distillation. From the first fraction there was isolated 1.6 g of a fraction b.p. 60.7-62.5°, containing chloroform as shown by the qualitative test with resorcinol and by the spectral data. Second and third fractions consisted mainly, as shown by the spectral data, of butyl chloride ($\lambda$ 7.55, 8.37, 10.30 and 10.67 $\mu$) and a small admixture of chloroform ($\lambda$ 7.0, 8.20 and 10.9 $\mu$).

By repeated vacuum distillation of the 13.3 g residue at 35 mm vacuum there was isolated 1.7 g of a substance with b.p. 193°, $d^0_0$ 1.338, $n^{20}D$ 1.4820.

Found %: C 30.1; H 4.1; Cl 65.0. M 198. $C_5H_8Cl_4$. Calculated %: C 28.6; H 3.8; Cl 67.7.

Pentachloroethane–Methanol. Thirteen and six tenths g (0.067 mole) of pentachloroethane and 6.4 g (0.200 mole) of methanol were heated 15 hours at 210-220°. There was evolved 3.6 g of a gas (the weight of gas was determined by weight difference of the tube before and after the release of the gases). The aqueous layer (2.4 ml) and the wash water contained 0.030 g of hydrogen chloride and 0.090 g of formaldehyde (m.p. of dimedone derivative 186°, without depression of mixed authentic sample). The mixture from seven tubes was taken for the analysis of the nonaqueous portion. The weight before washing was 131.9 g and after washing 117.6 g. After drying with potassium carbonate the mixture was distilled through the column. There were isolated the fractions: 1st 83.5-96.0°, 4.0 g; 2nd 99.5-125.5°, 3.0 g; 3rd 133.0-140.0°, 3.1 g; 4th 145-147°, 1.0 g; 5th 155-161°, 12.7 g; 6th 161-165.0°, 44.2 g; residue 10 g. Ten grams of methyl chloride was isolated in addition during the distillation. The first fraction contained trichloroethylene, $d^{20}$ 1.441, $n^{17}D$ 1.4720.

Found %: Cl 79.74 . M 128. $C_2HCl_3$. Calculated %: Cl 80.98. M 131.

The identify of trichloroethylene was proved by the preparation of the organomercury compound $Hg(CCl = CCl_2)_2$ by the reaction with mercuric cyanide.

Found %: Hg 42.9; Cl 45.5. M 445. $C_4Cl_6Hg$. Calculated %: Hg 43.4; Cl 46.2. M 461.

The second fraction was examined for the content of tetrachloroethylene by its reaction with bromine in carbon tetrachloride. No absorption of bromine was observed and a solution of potassium permanganate was not decolorized. The fourth fraction contained 1,1,2,2-tetrachloroethane ($n^{12}D$ 1.491, $d^{20}_D$ 1.590).

Found %: Cl 82.40. M 165. $C_2H_2Cl_4$. Calculated %: Cl 84.52. M 168.

The sixth fraction was unreacted pentachloroethane ($d^0_0$ 1.710, $n^{20}D$ 1.505).

**1,1,2,2-Tetrachloroethane–Methanol.** Tetrachloroethane (12.8 g; 0.076 mole) and 7.1 g (0.211 mole) of methanol were heated 12-15 hours at 210-215°. No layering of the liquid was observed. Heating for 12 hours at 220-230° did lead to layer formation. There was isolated 0.6 g of methyl chloride. The 2.3 ml, aqueous layer contained 0.004 g of hydrogen chloride while the wash water was neutral. There was found 0.03 g of formaldehyde (dimedone derivative, m.p. 187°). The nonaqueous part was analyzed after combining the contents of six tubes. The weight prior to washing was 100.15 g, and after washing it was 68.4 g. The latter weight was taken for the distillation. There were isolated the fractions: 1st 75.0-100.0°, 2.6 g, containing trichloroethylene (determined by the formation of $Hg(CCl=CCl_2)_2$); 2nd 100.0-139.0°, 2.6 g; 3rd 144.5°, 47.3 g containing unreacted tetrachloroethane (determined by b.p. and index of refraction); residue was 14.0 g.

**1,1,1,2-Tetrachloroethane–Methanol.** Tetrachloroethane (12.7 g; 0.076 mole) and 7.1 g (0.211 mole) of methanol were heated 12-15 hours at 215-220°. Considerable amount of tar was formed. The evolved gas (4.7 g) contained 1.1 g of methyl chloride. The aqueous layer (1.6 ml) and the wash water contained 0.035 g of hydrogen chloride. Traces of formaldehyde were detected. The nonaqueous part (from eight tubes) gave a stable emulsion on washing with water, this emulsion being broken by steam distillation, followed by drying with potassium carbonate, which gave 143.5 g of product. Distillation gave a fraction of 80-120°, 6.2 g, in which no trichloroethylene was detected (the mercury compound with mercuric cyanide failed to form as it did in previous examples). Neither was there isolated a fraction corresponding to trichloroethane. The weight of the tar after drying at 100° was 0.34 g (from one tube). On heating, the tar evolved hydrogen chloride. The content of chloride in the tar (by sodium fusion) was 23.3%.

## SUMMARY

1. The thermal reactions of carbon tetrachloride with 1-butanol and 2-butanol proceed with formation of hydrogen chloride, the appropriate dehydrogenation product of the alcohol (aldehyde or ketone) and chloroform.

2. Dehydrogenation of the alcohol to formaldehyde and formation of hydrogen chloride and tetrachloroethane, which in part loses hydrogen chloride and yields trichloroethylene, was observed after heating pentachloroethane with methanol, as it was with carbon tetrachloride.

3. On heating methanol with symmetric tetrachloroethane there takes place the decomposition of the latter with evolution of hydrogen chloride and trichloroethylene. Dehydrogenation of the alcohol was observed only to an insignificant degree.

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## LITERATURE CITED

[1] G. A. Razuvaev and N. S. Vasileiskaia, Doklady Akad. Nauk SSSR 80, 69 (1951).

[2] G. A. Razuvaev and Iu. A. Sorokin, J. Gen. Chem. 23, 1519 (1953).*

[3] K. Hannerz, Research 9 (1956).

[4] G. A. Razuvaev, B. N. Moryganov and V. A. Stepushkina, J. Gen. Chem. 23, 1376 (1953).*

[5] G. A. Razuvaev and N. S. Vasileiskaia, Sci. Notes of Gorky State Univ. 32, 175 (1958).

---

*Original Russian pagination. See C. B. Translation.

[6] G. A. Razuvaev and N. A. Osanova, J. Gen. Chem. 24, 1771 (1954).*

[7] D. H. R. Barton and P. F. Ongon, J. Am. Chem. Soc. 72, 988 (1956).

[8] J. Hanna and Si. Sigga, Anal. Chem. 22, 569 (1950).

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* Original Russian pagination. See C. B. Translation.

# UTILIZATION OF BENZENE AS A SOLVENT IN ACETYLATION REACTION ACCORDING TO FRIEDEL-CRAFTS

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It is evident on examination of the literature data [1-8] about the relative rates of heterolytic reactions in the series of benzene homologs that the reactivity of benzene is considerably lower than that of its alkyl derivatives (Table 1).

It follows from the data shown in Table 1 that the greatest difference in the rates of reaction of alkyl homologs of benzene as compared with benzene itself is observed in bromination, chlorination and chloromethylation; this difference is considerably smaller in reactions of nitration, sulfonation, mercuration and acetylation.

TABLE 1

Relative Rates of Certain Heterolytic Reactions of Monoalkylbenzene $C_6H_5-R$ (for benzene-1)

| Reaction | R | | | |
|---|---|---|---|---|
| | $CH_3$ | $C_2H_5$ | iso-$C_3H_7$ | tert-$C_4H_9$ |
| Bromination<br>($Br_2$ in $CH_3COOH$ at 25°) | 467 | 354 | 204 | 107 |
| Chlorination<br>($Cl_2$ in $CH_3COOH$ at 24°) | 345 | 290 | 176 | 110 |
| Chloromethylation<br>($CH_2O$ + HCl in $CH_3COOH$ at 60°) | 112 | — | — | — |
| Nitration<br>($HNO_3$ in $(CH_3CO)_2O$, $HNO_3$ + $H_2SO_4$ at 30°) | 23 | — | — | 15.7 |
| Mercuration<br>($Hg(OCH_3CO)_2$ in $CH_3COOH$) | 25 | — | — | — |
| Acetylation<br>($CH_3COCl$ + $AlCl_3$ at 0°) | 13.3 | — | — | — |
| ($CH_3COCl$ + $AlCl_3$ at 50°) | 8.4 | — | — | — |
| Sulfonation<br>(100% $H_2SO_4$ in $C_6H_5NO_2$ at 40°) | 5.1 | — | — | — |

The reduction of the relative reaction rate in the series of benzene homologs has the following dependence on the nature of the alkyl substituent: $CH_3$ > $C_2H_5$ > iso-$C_3H_7$ > tert-$C_4H_9$. The relative reactivity of these homologs of benzene in bromination and chlorination is considerably greater than it is in nitration.

It should be noted that the relative reaction rates in passage from toluene to tert-butylbenzene are decreased, respectively, by 4.35 and 3.14 fold in the reactions of bromination and chlorination, while in nitration the change is but 1.46 fold.

In the reactions of mercuration, acetylation and sulfonation of toluene the reactivity of the latter is of the same order as in the nitration reaction; therefore one should expect that in the above-cited reactions in the series of toluene-tert-butylbenzene there would be observed a regularity that is characteristic of nitration.

Since literature does not cite any comparative data on the reaction of acetylation in the series of alkyl homologs of benzene, it seemed interesting to clarify the possibility of running a selective acetylation of these substances in the presence of benzene in a Friedel-Crafts reaction. This should have a degree of significance for the preparative syntheses of methyl alkylaryl ketones, since the use of benzene as the solvent in this reaction is much more convenient than is the use of the fire-hazardous and toxic carbon disulfide or nitrated hydrocarbons. In addition, here one would find a more complete utilization of alkylated benzene derivatives.

The acetylation was run with acetic anhydride. The following ketones were prepared: acetophenone, p-methylacetophenone, p-ethylacetophenone, p-isopropylacetophenone, p-n-butylacetophenone, p-sec-butylacetophenone, p-tert-butylacetophenone as well as β-methyl-α-acetylnaphthalene.

## EXPERIMENTAL

The process of acetylation was run at 10° with the proportion of reactants being 0.5 mole of benzene homolog, 1 mole of benzene, 1 mole of acetic anhydride and 1.2 moles of aluminum chloride. The mixture of hydrocarbon with acetic anhydride was added to the suspension of aluminum chloride in benzene with stirring at such a rate that permitted one to maintain the reaction temperature at 10°. Then the mixture was stirred for one hour at the same temperature, the reaction products were poured into a mixture of ice and concentrated hydrochloric acid, the oily layer was separated, washed with water, aqueous solution of sodium carbonate, then again with water, dried over anhydrous calcium chloride and distilled in vacuum.*

TABLE 2

Properties of Products of Acetylation of Alkyl Homologs of Benzene p-$RC_6H_4COCH_3$ and the Melting Points of Their 2,4-Dinitrophenylhydrazones

| R | B.p. (pressure in mm) | Yield (in %) | Melting points of 2,4-dinitrophenylhydrazones | |
|---|---|---|---|---|
| | | | found | literature data |
| H . . . . . | 95° (20) | 6.7 | 249—250° | 249° [9] |
| $CH_3$ . . . . | 120 (20) | 85.0 | 258—259 | 260 [10] |
| $C_2H_5$ . . . | 86 (3) | 74.0 | 209 | 208—209 [11] |
| iso-$C_3H_7$ | 100 (3) | 70.0 | 185 | 185—186 [11] |
| n-$C_4H_9$ . . | 112 (3) | 65.0 | 160 | 160 [12] |
| sec.-$C_4H_9$ | 122 (3—4) | 62.0 | 145—147 | 145—146 [11] |
| tert.-$C_4H_9$ | 135 (20) | 60.0 | 212 | 212.5—213.5 [11] |

The yields of the ketones prepared by the above method, as well as some of their physicochemical properties and the melting points of the corresponding 2,4-dinitrophenylhydrazones are shown in Table 2.

It is interesting to note that practically no formation of ortho- or meta-isomers was detected under the selected conditions of acetylation.

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* The content of the ketone in the reaction mixture was determined in parallel by oximation.

Besides the indicated ketones there was obtained $\beta$-methyl-$\alpha$-acetylnaphthalene by acetylation, under the same conditions, of $\beta$-methylnaphthalene in yield of 67% of theoretical. The product was an oil with b.p. 168-169° at 3 mm, $n^{24}_D$ 1.6206, which was not identified any further. Simultaneously with the $\beta$-methyl-$\alpha$-acetylnaphthalene there was obtained acetophenone (from the benzene used as the solvent) in a yield of about 20% of theoretical.

## SUMMARY

1. It was shown that in acetylation according to Friedel-Crafts of benzene and a series of its homologs, the reactivity of the latter exceeds considerably the reactivity of benzene itself.

2. The difference in reactivity of benzene and its alkyl homologs permits the use of benzene as the solvent for acetylation according to Friedel-Crafts method.

## LITERATURE CITED

[1] De la Mare and J. Robertson, J. Chem. Soc. 1943, 279.

[2] W. M. Schubert and W. A. Sweeny, J. Org. Ch. 21, 119 (1956).

[3] K. le Roi Nelson, J. Org. Ch. 21, 145 (1956).

[4] C. Ingold, A. Lapworth, et al., J. Chem. Soc. 1931, 1959.

[5] A. Cohn, E. Hughes, G. Jones and R. Peeling, Nature 169, 261 (1952).

[6] A. Holleman and A. Caland, Ber. 44, 2504 (1911).

[7] O. Jacobson, Ber., 14, 2624 (1881).

[8] H. C. Brown, H. W. Pearsall, L. P. Eddy, W. J. Wallace, M. Grayson and K. le Roi Nelson, Ind. Eng. Ch. 45, 1462 (1953).

[9] W. S. Johnson, R. D. Shennan and R. A. Reid, Organic Reagents for Organic Analysis, Foreign Literature Press, p. 155 (1948).*

[10] R. Shriner and R. Fuson, Systematic Qualitative Analysis of Organic Compounds, p. 260 (1950).**

[11] H. Pines and A. W. Shaw, J. Org. Ch. 20, 374 (1955).

[12] V. N. Ipatieff et al., J. Am. Chem. Soc. 75, 3323 (1953).

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*Russian translation.

**In Russian.

# ACCELERATING EFFECT OF AMINES ON ISOTOPE EXCHANGE OF SULFUR IN ORGANIC POLYSULFIDES

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It is known that some amines show an accelerating action on chemical reactions with participation of elemental sulfur and organic polysulfides. There are literature data on acceleration of the process of addition of sulfur to diethyl disulfide in the presence of dibutylamine [1, 2]. There is information to the effect that diethylamine accelerates the addition of sulfur to cyclohexene [3], and that some amines aid the transition of polymeric sulfur into the soluble state [4, 5]. The accelerating effect [6-8] of amines on the process of sulfur vulcanization of rubber is also known. In one of our studies [9] there had been observed the accelerating action of dibutylamine on the isotope exchange of sulfur between diethyl trisulfide and elemental sulfur, as well as on the exchange of RS groups in polysulfides. However, a more systematic examination of the problem of the effect of composition and structure of the amines on their catalytic activity in the reactions in which sulfur participates was not made at that time.

One may take any of the above listed systems, for example the reaction of addition of sulfur to disulfide RS—SR with formation of RS—S—SR and other polysulfides, a reaction that had been studied in some detail [2] in cases of addition of sulfur to diethyl disulfide in the presence of dibutylamine, for the study of comparative activity of amines differing in composition and structure. However, it is quite difficult, and sometimes impossible, to run a quantitative analysis of such systems containing a mixture of products with similar constants.

We attempted in this work to carry out a comparison of activity of various amines by the way of study of the reaction of isotope exchange of sulfur between organic polysulfides and elemental sulfur. Apparently the mechanism of the activating action of the amines on sulfur and polysulfides in the systems examined above is the same and therefore the reaction of isotope exchange of sulfur may be regarded as being a model reaction.

Exchange ability of sulfur in organic polysulfides depends to a great extent on the composition and the structure of the radicals R and on the number of sulfur atoms in the polysulfide bridge [9]. The polysulfides with aliphatic radicals possess stronger polysulfide bonds and are less susceptible to exchange than are polysulfides with aromatic radicals. Introduction of a methylene group between the phenyl ring and the polysulfide bridge leads to the phenomenon in which the exchange of sulfur, for example in dibenzyl trisulfide $C_6H_5CH_2-S-S-S-CH_2-C_6H_5$ proceeds under conditions which are close to those needed for sulfur exchange in polysulfides with aliphatic radicals. The exchange ability rises with increased number of atoms of sulfur in the polysulfide.

For making this study we took polysulfides in which the sulfur exchange takes place under relatively drastic conditions: dibenzyl trisulfide and diethyl trisulfide.

It had been shown earlier [10] that only the middle atom of sulfur is the exchangeable sulfur atom in these polysulfides.

$$RS-S-SR + \overset{*}{S} \rightarrow RS-\overset{*}{S}-SR + S$$

Addition of certain amines brings about a considerable change in the conditions for sulfur exchange in these compounds, which fact permitted us to compare the activities of various amines.

It should be noted that such reactions of exchange are accompanied by addition of sulfur and by formation of higher polysulfides. The analysis of a mixture of polysulfides is as complicated a matter as in the reactions cited above. However, it is possible to secure quite single-valued data on the rate of the progress of the reaction by analyzing the activity of elemental sulfur. Alteration of activity of sulfur may take place only as the result of exchange with the middle sulfur atom of the polysulfide. Considering that the exchangeability of polysulfides, which are richer in sulfur, in much greater, the addition of active sulfur will change only the amount of residual free sulfur and will not affect its activity. The decompositions of the trisulfides with evolution of sulfur do not take place under the experimental conditions used by us. The correctness of these hypotheses was checked by us experimentally by making a balance sheet of radioactivity. We used the radioactive isotope of sulfur $S^{35}$ for the labelled atom.

Experiments with isotope exchange were run in sealed ampoules in toluene in nitrogen atmosphere. The concentration of solutions was 0.28 moles per liter of trisulfide and 0.28 gram-atoms per liter of radioactive sulfur. All exchange accelerators were taken in the amount equal to 5% of the trisulfide weight. The separation of the components after the exchange was done as follows. The solvent was evaporated in the cold (by means of a nitrogen flow) and the residual mass was treated with acetone; here the trisulfide, the higher polysulfides and also amines went into solution, while sulfur remained mainly undissolved. After 2- or 3-fold washing with acetone, the sulfur was recrystallized from benzene and a known sample (about 0.01 g) was oxidized by the Carius method and was precipitated with benzidine hydrochloride. The activity of the precipitates of benzidine sulfate was determined. In some of the experiments the trisulfide was isolated from the mixture for a control: in case of dibenzyl trisulfide this was done by fractional crystallization from alcohol, while in the case of diethyl trisulfide it was separated by vacuum fractionation; the activity of sulfur in these compounds after the exchange was then determined. Part of the specimens used in the work: dibenzyl trisulfide, diethyl trisulfide, sodium diisobutyldithiocarbamate, piperidine cyclopentamethylenedithiocarbamate, were synthesized by us, while the remaining specimens were taken in ready state. All these substances were additionally purified and had characteristics which corresponded to the literature data.

The results of experiments with sulfur exchange between dibenzyl trisulfide and elemental sulfur, as well as between diethyl trisulfide and elemental sulfur in the absence of accelerators are given in Table 1.

TABLE 1

| Temp. | Time (hours) | Activity of sulfur (cts./min) | | Percentage of exchange |
|---|---|---|---|---|
| | | before exchange | after exchange | |
| | | Dibenzyl trisulfide – sulfur | | |
| 80° | 1 | 2610 | 2600 | 0 |
| 100 | 1 | 1900 | 1900 | 0 |
| 100 | 2 | 2608 | 2610 | 0 |
| 120 | 1 | 2610 | 2505 | 4 |
| 120 | 2 | 2730 | 2510 | 16 |
| 140 | 1 | 1900 | 1450 | 15 |
| 200 | 1 | 1900 | 908 | 100 |
| | | Diethyl trisulfide – sulfur | | |
| 75 | 2 | 2360 | 2370 | 0 |
| 90 | 2 | 2360 | 2360 | 0 |
| 100 | 2 | 2180 | 2170 | 0 |
| 125 | 2 | 2180 | 1930 | 23 |

It is evident that sulfur exchange in the trisulfides studied by us begins in the absence of accelerators only at 120°. Considering the data shown in Table 1 we selected the time interval of two hours as the standard. The analysis of the products after exchange was run in all experiments two hours after the beginning of the reaction.

The results of experiments with sulfur exchange between dibenzyl trisulfide and radioactive sulfur in the presence of various amines are shown in Table 2. Analogous data for the diethyl trisulfide are given in Table 3. The names and the formulas of the amines used by us and the percentage of exchange at the indicated temperatures are shown in the tables.

TABLE 2

Dibenzyl Trisulfide—Sulfur

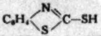
| No. | Exchange accelerator |  | Percentage of exchange |  |  |  |
|---|---|---|---|---|---|---|
|  | name | formula | 25° | 41° | 75° | 125° |
| 1 | Without accelerator | — | 0 | 0 | 0 | 16 |
| 2 | n-Propylamine | $C_3H_7NH_2$ | 77 | 100 | — | — |
| 3 | Isobutylamine | $(CH_3)_2CHCH_2NH_2$ | — | 66 | 100 | — |
| 4 | n-Amylamine | $C_5H_{11}NH_2$ | 43 | 62 | 86 | — |
| 5 | n-Heptylamine | $C_7H_{15}NH_2$ | 27 | 41 | 70 | — |
| 6 | Aniline | $C_6H_5NH_2$ | 0 | 0 | 0 | 12 |
| 7 | Diethylamine | $(C_2H_5)_2NH$ | — | 64 | — | — |
| 8 | Di-n-propylamine | $(C_3H_7)_2NH$ | — | 88 | — | — |
| 9 | Di-n-butylamine | $(C_4H_9)_2NH$ | 90 | 100 | — | — |
| 10 | Di-n-amylamine | $(C_5H_{11})_2NH$ | 74 | 100 | — | — |
| 11 | Dibenzylamine | $(C_6H_5CH_2)_2NH$ | 0 | 0 | 7 | 80 |
| 12 | Diphenylamine | $(C_6H_5)_2NH$ | 0 | 0 | 0 | 16 |
| 13 | Tri-n-butylamine | $(C_4H_9)_3N$ | 0 | 0 | 43 | 90 |
| 14 | Triisobutylamine | $(C_4H_9)_3N$ | 0 | 0 | 35 | 88 |
| 15 | Tri-n-amylamine | $(C_5H_{11})_3N$ | 0 | 0 | 0 | 72 |
| 16 | Tribenzylamine | $(C_6H_5CH_2)_3N$ | 0 | 0 | 0 | 16 |
| 17 | Dimethylaniline | $C_6H_5(CH_3)_2N$ | 0 | 0 | 0 | 14 |
| 18 | 2-Mercaptobenzothiazole |  | 0 | 0 | 0 | 14 |
| 19 | Tetramethylthiuram disulfide | $(CH_3)_2N{-}CS{-}S{-}S{-}CSN(CH_3)_2$ | 0 | 0 | 0 | 37 |
| 20 | Sodium diisobutyldithiocarbamate | $(C_4H_9)_2N{-}CS{-}SNa$ | — | — | 92 | 100 |
| 21 | Piperidine cyclopentamethylenedithiocarbamate | $C_5H_{10}N{-}CS{-}SH \cdot HNC_5H_{10}$ | — | 85 | 100 | — |

TABLE 3

Diethyl Trisulfide—Sulfur

| No. | Exchange accelerator |  | Percentage of exchange |  |  |  |
|---|---|---|---|---|---|---|
|  | name | formula | 25° | 41° | 75° | 125° |
| 1 | Without accelerator | — | 0 | 0 | 0 | 23 |
| 2 | Isobutylamine | $(CH_3)_2CHCH_2NH_2$ | 61 | 100 | — | — |
| 3 | Aniline | $C_6H_5NH_2$ | 0 | 0 | 0 | 26 |
| 4 | Di-n-butylamine | $(C_4H_9)_2NH$ | — | 90 | 100 | — |
| 5 | Dibenzylamine | $(C_6H_5CH_2)_2NH$ | 0 | 21 | — | 92 |
| 6 | Tri-n-butylamine | $(C_4H_9)_3N$ | — | — | 33 | 94 |
| 7 | Tetramethylthiuram disulfide | $(CH_3)_2N{-}CS{-}S{-}S{-}CS{-}N(CH_3)_2$ | 0 | 0 | 0 | 43 |
| 8 | Sodium diisobutyldithiocarbamate | $(C_4H_9)_2N{-}CS{-}SNa$ | 54 | 75 | — | — |
| 9 | Piperidine cyclopentamethylenedithiocarbamate | $C_5H_{10}N{-}CS{-}SH \cdot HNC_5H_{10}$ | 92 | 100 | — | — |
| 10 | p-Nitroaniline | $NO_2C_6H_4NH_2$ | 0 | 0 | 0 | 5 |
| 11 | Diphenylguanidine | $(C_6H_5NH)_2C{=}NH$ | 40 | 77 | 96 | 100 |
| 12 | Monoethanolamine | $NH_2CH_2CH_2OH$ | 0 | 0 | 25 | 75 |
| 13 | Diethanolamine | $NH(CH_2CH_2OH)_2$ | 0 | 30 | 64 | 100 |
| 14 | Triethanolamine | $N(CH_2CH_2OH)_3$ | 0 | 0 | 15 | 70 |

It is evident from comparison of data in Tables 1-3 that the catalytic activity of various amines depends considerably on their composition and structure.

In the series of simple amines (compounds 2-17 in Table 2 and 2-6 in Table 3) the primary and the secondary amines with aliphatic radicals are most active. Addition of a small amount (about 5%) of such amines to the system makes the latter exchangeable even at room temperature while in the absence of the amines the exchange takes place only with difficulty at 125°.

Among primary amines the dependence of catalytic activity on the radical length is clearly displayed: the longer the aliphatic chain the less active is the amine. The amines studied by us (substances 2-5 in Table 2) may be arranged according to the accelerating action in the following series: $C_3H_7NH_2 > C_4H_9NH_2 > C_5H_{11}NH_2 > > C_7H_{15}NH_2$. Among secondary amines (substances 7-10 in Table 2) no such regularity is observed.

Tertiary amines with aliphatic radicals (substances 13-15 in Table 2) are considerably less active than are the primary and the secondary amines. The accelerating effect of these amines is shown only at a temperature about 70°.

Aromatic amines, such as primary ones – aniline (substance 6 in Table 2 and substance 3 in Table 3), as well as secondary ones – diphenylamine (substance 12 in Table 2) as tertiary ones – dimethylaniline (substance 17 in Table 3) do not accelerate the exchange at all. The sulfur exchange proceeds in their presence just as its does in the pure system: at 125° the extent is 12-16%.

As to benzylamines, they occupy an intermediate position between the corresponding aliphatic and aromatic amines. Dibenzylamine (substance 11 in Table 2 and substance 5 in Table 3) is considerably less active than are aliphatic secondary amines and more active than diphenylamine. Just as with the aliphatic compounds, the secondary amine – dibenzylamine – is more active than tertiary tribenzylamine.

Rather interesting was the fact that such ultraaccelerators of rubber vulcanization as sodium diisobutyldithiocarbamate (substance 20 in Table 2 and substance 8 in Table 3) and piperidine cyclopentamethylenedithiocarbamate (substance 21 in Table 2 and substance 9 in Table 3) are active accelerators of sulfur isotope exchange. Evidently the elemental acts of the reactions between the accelerators and sulfur, which lead to rubber vulcanization on one hand and to isotope exchange on the other hand, are one and the same, whereby the parallelism is quite natural.

The high temperature vulcanization accelerators: mercaptobenzothiazole (substance 18 in Table 2), thiuran (substance 19 in Table 2 and substance 7 in Table 3) practically do not accelerate the exchange under the conditions of the experiments at 120° or below. However, at 125° thiuram turned out to be more active than mercaptobenzothiazole. This fact agrees well with the data on isotope exchange of sulfur in these compounds: thiuram begins to exchange with elemental sulfur at a noticeable rate at 110° while mercaptobenzothiazole reacts with sulfur at a higher temperature (about 130-135°).

Diphenylguanidine (substance 11 in Table 3) is close in its properties to primary and secondary aliphatic amines and is a very active accelerator of exchange.

Mono- and di-ethanolamines (substances 12 and 13 in Table 3) are considerably less active than the simple primary and secondary amines with aliphatic radicals. Triethanolamine has the same activity as tertiary amines with aliphatic radicals.

It was interesting to follow up the change of activity of aromatic amines after introduction of polar substituents into the aromatic ring. We examined the accelerating activity of p-nitroaniline (substance 10 in Table 3). It turned out that this amine, just as aniline, completely fails to accelerate the exchange reaction.

It should be noted that the results obtained in this work relative to the great difference in activity of amines with aliphatic and aromatic radicals are in complete agreement with the data in a series of publications [2, 11] on the study of the reaction of addition of sulfur to diethyl disulfide in the presence of amines.

While in paper [2] there was observed a considerable activating effect of an aliphatic amine – dibutylamine – on the reaction of addition of sulfur to diethyl disulfide, it was found in paper [11] that aromatic amines – aniline and dimethylaniline – do not accelerate this reaction at all.

An analogous observation about the decrease of activity of amines after introduction of aromatic radicals into them was made in paper [12] in a study of vulcanizing activity of benzothiazolesulfenamides. The authors found that the accelerating reaction of these compounds depends on the nature of the substituent in the amino group. Introduction of aromatic radicals sharply lowers the activity of these compounds as vulcanization accelerators.

The problem of the mechanism of the accelerating action of amines on reactions in which polysulfides and elemental sulfur take part has been partially examined in the literature [1, 4, 5]. Some considerations have been expressed. Thus, Weslake and co-workers [1] observing the activating action of dibutylamine on the reaction of addition of sulfur to diethyl disulfide expressed the supposition that the amine weakens the S−S bond in the disulfide and thus aids the addition of sulfur. They also did not exclude the possibility of formation of RS radicals under the influence of the amine, followed by the addition of sulfur to these radicals.

According to Krebs' concepts [4, 5] amine in passing into the ammonium state ruptures the S−S bonds of sulfur, forming peculiar aminopolysulfides with an ionogenic termination, with the type $R_3N^+-S-S-S-S-S-$ $-S-S-S^-$. Such a complex may realize several acts of addition of sulfur and the rate of the process may be sufficiently great.

However, such schemes are purely imaginary, are not confirmed by any experimental facts, and have been expressed on the basis of isolated individual observations.

From analysis of the results shown in Tables 2 and 3 one may conclude that Krebs' scheme cannot be accepted for the basis of an explanation of the observed regularities. Actually, if the basic factor in the accelerating effect of amines is the transition into the ammonium state, one should expect that tertiary amines, which form quaternary ammonium compounds most readily, should not be less active than primary and secondary amines. It was established experimentally that tertiary amines are considerably less active. In addition, it is known that aromatic amines are also capable of forming ammonium compounds and, according to Krebs' scheme they ought to be active accelerators. But as shown by the experimental data, aromatic amines are completely inactive in these processes up to 125°. The circumstance that among amines the most active are those compounds with aliphatic radicals which have an unsubstituted hydrogen atom in the amino group calls for some attention. Evidently a mobile hydrogen atom in the amine plays a rather important role in these processes. Evidently the low activity of aromatic amines, in comparison with the aliphatic ones, is caused by the different mobility of hydrogen atoms in them.

We attempted to obtain some data on the character of complexes formed by amines with sulfur and polysulfides, through the experimental route.

If the basis for the accelerating action of amines is the formation of ammonium compounds of the type such as $R_3N^+-S-S-S-S-S^-$, then one may hope to discover such complexes by measurement of the dipole moments. We measured the dipole moment of dibutylamine in benzene in the presence of sulfur at 25°, as well as the dipole moment of equimolar mixture of an amine and sulfur maintained at 100° for ten hours. No material changes of polar properties of these solutions were observed by us in comparison with the additive magnitude. Values close to additive ones were also obtained in the measurement of dipole moment of equimolar mixture of dibutylamine and diethyl trisulfide. In the calculation for the complex $(C_4H_9)_2NH \cdot (C_2H_5)_2S_3$ there were obtained the following results: 2.3 D for a mixture maintained at 25°, and 2.4 D for a mixture heated at 100° for five hours. The additive scheme in a parallel distribution of the dipoles of dibutylamine (1.03 D) and diethyl trisulfide (1.64 D) gives the maximum value of 2.67 D for the complex, i.e., one that is close to the experimental result. Consequently, the formation of any notable amounts of polar complexes in the systems under study was not observed.

The cited material, both purely chemical and physicochemical, seems to us to be completely adequate for the conclusion that the accelerating action of amines is not connected with their transition into the ammonium state. Evidently the reaction of amines with sulfur and polysulfides has a homolytic rather than heterolytic character.

We attempted to use diphenylpicrylhydrazyl (DFPG) as an indicator for the radicals in the systems under study. Solutions of sulfur and diethyl trisulfide in benzene do not decolorize the diphenylpicrylhydrazyl (0.001 N) at 25° for a very long time (over 4 days). Dibutylamine in benzene reacts slowly with DFPG. Addition to the dibutylamine solution of a solution of sulfur or diethyl trisulfide considerably (more than twice) accelerates the reaction with DFPG. These, thus far purely qualitative, results permit us to make the preliminary conclusion about the radical mechanism of the accelerating action of amines.

Clarification of the nature of the reaction of amines with sulfur, as well as with organic polysulfides, inorganic polysulfides and other sulfur-bearing compounds, has a considerable interest, since these reactions lie in the foundation of such most important technological processes as rubber vulcanization, preparation of sulfur dyes, etc. This problem, as may be seen from the above, remains unclarified to this day.

Rather valuable data on the character of the reaction of amines with sulfur and polysulfides may be evidently obtained by a study of the vibrational and electronic spectra of these systems. Work in this direction will be continued in the future.

## SUMMARY

1. The effect of composition and structure of amines on the acceleration of the reaction of isotopes exchange of sulfur between dibenzyl trisulfide and radioactive sulfur (elemental), as well as between diethyl trisulfide and elemental sulfur, were studied. The accelerating action of 26 different compounds on this exchange was investigated, among these compounds being a series of industrial rubber vulcanization accelerators.

2. It was shown that ultra-accelerators of rubber vulcanization – piperidine cyclopentamethylenedithiocarbamate and sodium diisobutyldithiocarbamate – are active exchange accelerators. High temperature vulcanization accelerators – mercaptobenzothiazole and thiuram – practically do not accelerate the exchange under the experimental conditions used (120°).

3. The polar properties (dipole moments were measured) of s number of systems under study were explored and some conclusions were made as to the mechanism of the reaction of amines with sulfur and polysulfides.

## LITERATURE CITED

[1] H. E. Weslake, U. L. Laquer and C. D. Smyth, J. Am. Chem. Soc. 72, 486 (1950).

[2] E. N. Gur'ianova, Ia. K. Syrkin and L. S. Kuzina, Doklady Akad. Nauk SSSR 85, 1021 (1952).

[3] S. Moore, J. Chem. Soc. 1954, 2082.

[4] H. Krebs, Z. anorg. allg. Chem. 27, 288 (1953).

[5] H. Krebs, Gummi u. Asbest, 2, 68 (1955).

[6] U. S. Patent 2,684,391 (1954).

[7] U. S. Patent 2,603,168 (1952).

[8] B. A. Dogadkin, Chemistry and physics of rubber, State Chem. Press, 1947.*

[9] E. N. Gur'ianova, V. N. Vasil'eva and L. S. Kuzina, Meeting on use of atomic energy for peaceful purposes. Published by Academy of Sciences USSR, p. 270 (1955). *

[10] E. N. Gur'ianova, J. Phys. Chem. USSR 28, 67 (1954).

[11] M. P. Tikhomolova, Dissertation: A study of polymerization of chloroprene in solutions, Leningrad, 1954.*

[12] B. A. Dogadkin, N. A. Strel'nikov, M. S. Fel'dshtein, T. P. Shcherbachev and N. I. Eitigon, Reports of conference on problems of vulcanization of rubber articles (1956).*

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# SYNTHESIS OF 2-ETHYLANTHRONE AND 2-ETHYL-10-OXANTHRONE LABELED WITH CARBON $C^{14}$ IN THE NUCLEUS AND A STUDY OF SOME OF THEIR PROPERTIES

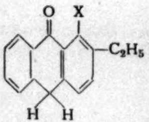
S. V. Siavtsillo, V. I. Savushkina and E. M. Zhernovskaia

2-Ethylanthrone, labeled with carbon $C^{14}$ in the nucleus was synthesized by reduction of 2-ethylanthraquinone labelled with carbon $C^{14}$ [1]. The reduction was run analogously to that of anthrone [2]. 2-Ethylanthrone was obtained in the pure state (m.p. 62°) and did not contain the enolic form; it did not tautomerize after prolonged standing in the solid state or in benzene solutions. Previously [3] 2-ethylanthrone had been obtained only in a mixture with 2-ethylanthranol by solution of 4-ethyldiphenylmethanecarboxylic acid in concentrated sulfuric acid. The product had m.p. 67-75°.

From 2-ethylanthrone labeled with carbon $C^{14}$ there was prepared the previously undescribed 2-ethyl-10-oxanthrone (m.p. 92-3°) by the scheme used by Meyer [4] in the synthesis of oxanthrone, i.e., by the way of bromination of 2-ethylanthrone with a subsequent hydrolysis of 2-ethyl-10-bromoanthrone labeled with carbon $C^{14}$. In order to avoid the formation of products of oxidation, the bromination of 2-ethylanthrone and isolation of 2-ethyl-10-bromoanthrone were run at a low (from −8° to −20°) temperature.

For hydrolysis of 2-ethyl-10-bromoanthrone there was used a more concentrated (75%) aqueous solution of acetone and the recrystallization of 2-ethyl-10-oxanthrone was done from a mixture of solvents taken in definite proportion. 2-Ethyl-10-oxanthrone is stable in the solid state and tautomerizes on standing in benzene, alcoholic and alkaline solutions.

## EXPERIMENTAL



(A)

2-Ethylanthrone. (A). Into a round bottom flask with a reflux condenser, a thermometer and a dropping funnel there was charged a mixture consisting of 13 g (110 millimoles) of granulated tin, 11.2 g (47 millimoles) of 2-ethylanthraquinone (activity 33 $\mu$Cu) and 80 ml of glacial acetic acid. The flask contents were heated to 120-130° and into the boiling mixture there was added 42 g of hydrochloric acid (d 1.17) over a one hour period. The mixture was kept at this temperature for half an hour, the hot solution being then filtered through a funnel with a porous glass plate.

Three hundred ml of water was added to the filtrate; the oily lower layer which separated was extracted with ether, the ethereal solution being then washed with water to a neutral reaction and was then dried with freshly roasted sodium sulfate. Crystalline 2-ethylanthrone was isolated on mixing the ethereal solution with petroleum ether, both precooled with solid carbon dioxide. The precipitate was filtered off through a chilled (with solid carbon dioxide) filter with a porous glass plate, and was washed with petroleum ether, after which it was dried in a vacuum desiccator. After a second crystallization there was obtained 5.6 g of 2-ethylanthrone in the form of white needles with m.p. 60-62°.

The yield based on radioactivity in the original 2-ethylanthraquinone was 49%. The determination of activity has been described before [5].

Found %: C 86.39; H 6.40. $C_{16}H_{14}O$. Calculated %: C 86.50; H 6.30.

Ultraviolet absorption spectra of 0.001 molar solution of the substance in carbon tetrachloride and of anthrone (m.p. 152° [2]) were taken for the identification of the compound synthesized by us; the SF-4 spectrophotometer was used.*

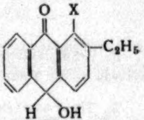
The compound prepared by us had a spectrum that was identical with that of anthrone in the region from 3500 to 2500 A; this confirms the fact that the compound is 2-ethylanthrone and not 2-ethylanthranol.

2-Ethylanthrone did not change on standing in air for several months in the solid state or in benzene solutions. It is readily soluble in benzene without fluorescence, in methyl alcohol with blue fluorescence, and is noticeably soluble in 5% aqueous solution of sodium hydroxide with bright green fluorescence. The latter phenomenon is explained by the fact that 2-ethylanthrone, in contrast with anthrone [6], suffers a tautomeric transformation into 2-ethylanthranol, which rapidly oxidized to 2-ethylanthraquinone, even at room temperature in aqueous alkaline solution.

2-Ethylanthranyl Acetate. 2-Ethylanthrone (1 g) was refluxed in a flask with a reflux condenser with 1 ml of glacial acetic acid and 7 ml of pyridine for two hours in a stream of carbon dioxide. Diluted with water the resulting solution gave an oil which solidified on cooling. After recrystallization from a mixture of ethyl and petroleum ethers there was obtained a lemon yellow precipitate with m.p. 90-92°.

Found %: C 81.37; H 6.31. $C_{18}H_{16}O_2$. Calculated %: C 81.80; H 6.06.

2-Ethyl-10-oxanthrone (B). To a solution of 2-ethylanthrone (2 g, activity 24.2 μ Cu) in carbon disulfide (100 ml) there was added 0.65 ml of bromine dropwise over forty minutes, at first at −8°, then at −15° to −20°. The resulting solution was filtered from the precipitated tarry material. The precipitate of 2-ethyl-10-bromoanthrone, which formed after the solution had been chilled with dry ice to −50° to −60°, was filtered through a funnel with a porous glass plate, chilled with dry ice, and the product was washed with chilled petroleum ether. M.p. 90-91°. Yield: 78%.



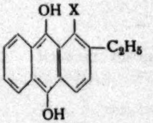
(B)

Found %: Br 26.13. $C_{16}H_{13}OBr$. Calculated %: Br 26.55.

The resulting 2-ethyl-10-bromoanthrone (2.3 g) was gradually heated with stirring at reflux in 75% solution of acetone (120 ml) until it dissolved completely. After dilution of the solution with ten volumes of water followed by standing for 2-3 hours, there formed a precipitate with light yellow color, which was filtered off, washed with water and dried in a vacuum desiccator. The resulting compound (1.52 g) with m.p. 88-90° was 2-ethyl-10-oxanthrone with admixture of 2-ethylanthraquinone. After recrystallization from a mixture of benzene (20 ml) and petroleum ether (60 ml) chilled to −10°, there was obtained 1.3 g of 2-ethyl-10-oxanthrone with m.p. 92-93°. The yield based on radioactivity of initial 2-ethylanthrone was 59%.

Found %: C 80.53; H 6.16. $C_{16}H_{14}O_2$. Calculated %: C 80.65; H 5.92.

2-Ethyl-10-oxanthrone forms white needles; it does not change on standing for five months in air. It is readily soluble in benzene, alcohol and ether and is insoluble in petroleum ether. It isomerized gradually to 2-ethylanthrahydroquinone (C), which oxidized in air to 2-ethylanthraquinone, in solutions in benzene and methyl alcohol at room temperature.



(C)

An analogous isomerization of 2-ethyl-10-oxanthrone was observed on heating in 5% aqueous solution of alkali, when an intense red coloration of the solution appeared. On oxidation of the alkaline solution there was isolated some 2-ethylanthraquinone.

2-Ethyl-10-oxanthrone standing in benzene solution over Raney nickel catalyst in nitrogen atmosphere at 20° isomerized in 180 hours to the extent of about 50% into 2-ethylanthrahydroquinone, while at 60° this reaction proceeded completely in the course of six hours.

Hydrogenation of 2-ethylanthrone and 2-ethyl-10-oxanthrone. On hydrogenation of 2-ethylanthrone (5 g) in benzene solution (50 ml) in the presence of Raney nickel at

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* The work was done by K. K. Popkov.

60° over 20 hours there was observed the absorption of hydrogen and formation of a red oil. After repeated fractional crystallization from various solvents there was isolated 2-ethylanthraquinone with m.p. 104-106° and 2-ethylanthracene with m.p. 155-156°. The formation of 2-ethylanthraquinone can be evidently explained by isomerization of 2-ethylanthrone into 2-ethylanthranol, in the process of hydrogenation, with subsequent oxidation of the latter in air to 2-ethylanthraquinone.

On hydrogenation of 2-ethyl-10-oxanthrone (1 g) in benzene (25 ml) under the same conditions there occurs the formation of 2-ethylanthrone (m.p. 60-62°), 2,2'-diethyl-10,10'-dihydrodianthrone (m.p. 190-192°), 2-ethylanthracene (m.p. 155-156°), 2-ethylanthraquinone (m.p. 104-106°) and 1,2,3,4-tetrahydro-2-ethylanthraquinone (m.p. 165-166°).

Oxidation of 2-ethylanthrone and 2-ethyl-10-oxanthrone. In oxidation of 2-ethylanthrone in benzene solution at 60° over six hours by atomic oxygen formed in the decomposition of hydrogen peroxide in the presence of Raney nickel, there is formed mainly 2,2'-diethyl-10,10'-dihydrodianthrone and an insignificant amount of 2-ethylanthraquinone.

In oxidation of 2-ethyl-10-oxanthrone with atomic oxygen in benzene solution at room temperature and at 60°, no noticeable uptake of oxygen was observed. The appearance of an insignificant amount of 2-ethylanthraquinone in this case can be explained by isomerization of 2-ethyl-10-oxanthrone.

## SUMMARY

1. 2-Ethylanthrone was synthesized and isolated for the first time in a form labeled with carbon $C^{14}$; the yield was 51%. There was prepared the acetate of 2-ethylanthranol (m.p. 90-92°).

2. There was synthesized the previously undescribed 2-ethyl-10-oxanthrone, labeled with carbon $C^{14}$ in the nucleus, in 59% yield.

3. The reactions of hydrogenation and oxidation of the indicated compounds were studied.

## LITERATURE CITED

[1] A. P. Terent'ev, S. V. Siavtsillo, V. I. Savushkina et al., Doklady Akad. Nauk SSSR, 107, 417 (1956).*

[2] Syntheses of organic compounds, vol. 1, 45 (1952).**

[3] R. Scholl, J. Potschiwanschen and J. Lenko, Monatsh. 32, 693 (1911).

[4] K. Meyer, Lieb. Ann. 379, 37 (1911).

[5] V. I. Savushkina, S. V. Siavtsillo and A. P. Terent'ev, Doklady Akad. Nauk SSSR 102, 1139 (1955).

[6] K. Nakado and V. Bausho, Bull. Soc. Chim., Japan, 26, 454 (1953).

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*Original Russian pagination. See C. B. Translation.

**In Russian.

# TETRAACYLOXYSILANES IN ORGANIC SYNTHESIS

## XVI. BENZOYLOXYTRICHLOROSILANE AND REACTIVITY OF BENZOYLOXY GROUP

Iu. K. Iur'ev and Z. V. Beliakova

An attempt to prepare acetoxytrichlorosilane by the action of an excess of silicon tetrachloride on acetic acid failed to give the desired reult, as reported by Goubeau and Mundiel [1], and the sole product of this reaction was tetraacetoxysilane; acetoxytrichlorosilane was prepared only by the action of silicon tetrachloride on sodium acetate. As to benzoyloxytrichlorosilane, this substance has not been prepared as yet.

In a series of studies on acylation of compounds of aromatic nature by means of tetraacetoxysilanes we prepared the latter by reaction of organic acids with silicon tetrachloride in a suitable solvent (benzene, nitrobenzene, carbon disulfide).

In a more detailed study of the reaction between silicon tetrachloride and benzoic acid we discovered that during the action of an excess of silicon tetrachloride on benzoic acid (molar ratios 1.7 : 1 and 2 : 1) in the absence of a solvent and with heating of the reaction mixture for twelve hours with a subsequent distillation of the reaction product in vacuum, there is formed a nearly quantitative yield of benzoyloxytrichlorosilane (I):

$$C_6H_5COOH + SiCl_4 \rightarrow C_6H_4COOSiCl_3 + HCl \qquad (I)$$

According to the data provided by Rauter [2] and Montonna [3] organic acids react with excess silicon tetrachloride on being heated in closed vessels to 150-160°, forming the corresponding chlorides of the acids and silica gel (II):

$$SiCl_4 + 4RCOOH \rightarrow 4RCOCl + [Si(OH)_4] \qquad (II)$$

The industrial method of preparation of benzoyl chloride from benzoic acid and silicon tetrachloride [4] is based on this reaction. It was supposed that the reaction proceeds through the stage of formation of tetraacyloxysilane (III) which under the further action of excess silicon tetrachloride yields the acyl chloride and silicon dioxide (IV):

$$4RCOOH + SiCl_4 \rightarrow Si(OCOR)_4 + 4HCl \qquad (III)$$

$$Si(OCOR)_4 + SiCl_4 \rightarrow 4RCOCl + 2SiO_2 \qquad (IV)$$

However, the data obtained by us indicate without a doubt that a reaction of this type proceeds by a more complex route.

Thus, by treating benzoic acid with excess silicon tetrachloride for five hours (the reagent proportion and the conditions of the reaction being exactly correspondent to those indicated in the paper by K. A. Andrianov) we then distilled the unreacted silicon tetrachloride on a steam bath and, having distilled the residue in vacuum, obtained a 36% yield of benzoyloxytrichlorosilane.

After heating benzoic acid with excess silicon tetrachloride for 4-5 hours and standing for 12 hours at room temperature there are separated some crystals of tetrabenzoyloxysilane.

On heating tetrabenzoyloxysilane on a water bath with excess silicon tetrachloride and distillation of the reaction product in vacuum, there is obtained a 53.5% yield of benzoyloxytrichlorosilane.

Benzoyloxytrichlorosilane is a colorless liquid which fumes in air and distills in vacuum with slight decomposition, analogously to acetoxytrichlorosilane, which is decomposed partially on being distilled in vacuum [1].

Distillation of benzoyloxytrichlorosilane at atmospheric pressure leads to its thermal decomposition into benzoyl chloride, silicon tetrachloride and silicon dioxide (V):

$$2C_6H_5COOSiCl_3 \rightarrow 2C_6H_5COCl + SiCl_4 + SiO_2 \qquad \text{(V)}$$

Distillation of a mixture of benzoyloxytrichlorosilane and tetrabenzoyloxysilane taken in the proportion required by the following equation also leads to formation of benzoyl chloride in 63% yield (VI):

$$2C_6H_5COOSiCl_3 + Si(OCOC_6H_5)_4 \rightarrow 6C_6H_5COCl + 3SiO_2 \qquad \text{(VI)}$$

The formation of benzoyl chloride should be represented not by Equation (IV) but by Equations (V) and (VI) as the result of reaction of benzoyloxytrichlorosilane and tetrabenzoyloxysilane (VI) which form in the reaction mixture, and thermal decomposition of the first of these on distillation at atmospheric pressure (V).

We note also that under the conditions indicated above for the preparation of benzoyloxytrichlorosilane and after the termination of this reaction (as shown by cessation of evolution of hydrogen chloride) we determined the amount of distilled silicon tetrachloride and established that only such an amount of it enters the reaction with benzoic acid as is called for by the stoichiometric proportion in Equation (I).

In our previous studies carried out jointly with G. B. Eliakov it was shown that tetraacyloxysilanes are excellent reagents for acylation of the nuclei of benzene [5], thiophene [6-8] and selenophene [9, 10]. The very possibility of the utilization of tetraacyloxysilanes for acylation of benzene according to the Friedel-Crafts reaction was first shown by K. D. Petrov and co-workers [11, 12].

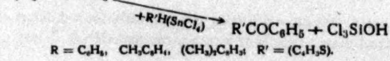
In connection with the above it appeared rather interesting, during the study of reactivity of benzoyloxytrichlorosilane, to study the possibility of acylation of compounds of aromatic nature by means of this substance. We ran an acylation of benzene with benzoyloxytrichlorosilane in the presence of anhydrous aluminum chloride and obtained benzophenone in yield of 73% (63.5% recalculated on the acid used to prepare benzoyloxytrichlorosilane). Since the distillation of benzoyloxytrichlorosilane, as indicated above, is accompanied by a slight decomposition, we ran the acylation of benzene with unpurified preparation, from which we only distilled the excess silicon tetrachloride under reduced pressure. In this case benzophenone was formed in a 70% yield, calculated on the acid used in the reaction with silicon tetrachloride. This fact indicates that benzoyloxytrichlorosilane proper is formed in nearly quantitative yield and that the yield of the pure substance amounts to only 88%, solely owing to the partial decomposition during distillation.

Thus, acylation of compounds of aromatic nature may be run also with undistilled benzoyloxytrichlorosilane, after the distillation from it of the excess silicon tetrachloride.

We obtained an 82% yield of a mixture of 2- and 4-methylbenzophenones by acylation of toluene with benzoyloxytrichlorosilane, from which mixture we isolated a 53% yield of 4-methylbenzophenone by repeated freezing-out, distillation and crystallization.

We obtained 2,4-dimethylbenzophenone (68%) by acylation of m-xylene.

Acylation of thiophene in the presence of anhydrous stannic chloride led to isolation of benzothienone in 70% yield.



$R = C_6H_5,\ CH_3C_6H_4,\ (CH_3)_2C_6H_3;\ R' = (C_4H_3S).$

It was interesting also to compare the reactivity of the benzoyloxy group and chlorine atoms in benzoyloxytrichlorosilane. It is known from the literature that during the action of alcohols on silicon tetrachloride, the chlorine atoms of the latter are readily replaced by the alkoxy groups with successive formation of alkoxytrichloro-, dialkoxydichloro-, trialkoxychloro- and tetraalkoxysilanes [13]. However the acyloxy group is also readily displaced by the alkoxy group, which was demonstrated by the reaction between butyl alcohol and methyltriacetoxysilane, which led to the formation of methylbutoxydiacetoxysilane and methyldibutoxyacetoxysilane [14].

We examined the action of ethyl alcohol on benzoyloxytrichlorosilane and established that the benzoyloxy group is replaced by the ethoxy group considerably more readily than are the chlorine atoms. To this fact we have the testimony of formation of benzoic acid in 69.5% yield, while molar amounts of the reactants were brought together at −25° to −30°. If the reactivities of the indicated groups were the same, the yield of the acid would have been but 25%.

At molar ratios of benzoyloxytrichlorosilane to ethyl alcohol of 1 : 3 and 1 : 4 the benzoic acid was obtained in yields of 80% and 88%, respectively, and along with it there was obtained tetraethoxysilane in yields of 38.5% and 45%, respectively.

$$C_6H_5COOSiCl_3 - \left| \begin{array}{l} \xrightarrow{+C_2H_5OH} C_6H_5COOH + C_2H_5OSiCl_3 + (C_2H_5O)_2SiCl_2 + HCl \\ \xrightarrow[+4C_2H_5OH]{} C_6H_5COOH + (C_2H_5O)_4Si + 3HCl \end{array} \right.$$

## EXPERIMENTAL

Preparation of benzoyloxytrichlorosilane: a) Into a flask with a reflux condenser there was placed benzoic acid and silicon tetrachloride and the mixture was heated on a water bath until hydrogen chloride ceased to form. After distillation of the unreacted silicon tetrachloride the residue was distilled in vacuum. The results obtained in these experiments are shown in the table.

| Expt. No. | Reaction components | | | | Duration of heating the mixture (hours) | Amount of unreacted $SiCl_4$ | | $C_6H_5COOSiCl_3$ isolated | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $C_6H_5COOH$ | | $SiCl_4$ | | | | | | | |
| | in g | in moles | in g | in moles | | in g | in moles | in g | in % of theory | b.p. (pressure in mm) |
| 1 | 12.2 | 0.1 | 29.6 | 0.17 | 12 | 8.9 | 0.052 | 22.3 | 87.5 | 112—113° * (12) |
| 2 | 12.2 | 0.1 | 34.0 | 0.20 | 12 | 17.0 | 0.10 | 22.5 | 88 | 116—117 (13) |
| 3 | 12.2 | 0.1 | 34.0 | 0.20 | 5 | 22.1 | 0.13 | 9.2 | 36 | 107—108 (10) |

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*Found %: Si 10.76, 10.81; Cl 41.58, 41.37. $C_7H_5O_2Cl_3Si$. Calculated %: Si 10.98; Cl 41.65.

After five hours of heating the reaction mixture and allowing it to stand 12 hours at room temperature (table, expt. 3) there precipitated some crystals (0.7 g) which were tetrabenzoyloxysilane with m. p. 41-42°; mixed melting point with authentic tetrabenzoyloxysilane gave no depression. Literature data: m. p. 42° [15].

b) To dry tetrabenzoyloxysilane, prepared by the method of K. D. Petrov and E. S. Lagucheva [9] from 12.2 g (0.1 mole) of benzoic acid and 5 g (0.03 mole) of silicon tetrachloride in 100 ml of dry benzene, there was added (after removal of benzene in vacuum) 30 g (0.175 mole) of silicon tetrachloride and the reaction mixture was heated for 12 hours on a water bath. After distillation of the unreacted silicon tetrachloride, the residue was distilled in vacuum. There was obtained 13.7 g (53.5%) of benzoyloxytrichlorosilane, b. p. 112-113° (12 mm).

Preparation of benzoyl chloride. a) To dry tetrabenzoyloxysilane, prepared from 5.86 g (0.048 mole) of benzoic acid and 2.4 g (0.014 mole) of silicon tetrachloride in 20 ml of benzene, there was added (after distillation of benzene in vacuum) 6.1 g (0.024 mole) of benzoyloxytrichlorosilane and the mixture was subjected to distillation at atmospheric pressure. There was obtained 6.6 g (64.5%) of benzoyl chloride, b. p. 194-195° (746 mm), $n^{20}D$ 1.5535, $d^{20}_4$ 1.212.

b) Under analogous conditions from the reaction of tetrabenzoyloxysilane (from 5.86 g of benzoic acid and 2.4 g of silicon tetrachloride) and 12.2 g (0.048 mole) of benzoyloxytrichlorosilane there was obtained 3.25 g (0.02 mole) of silicon tetrachloride (b. p. 56-57°) and 8.5 g (63.5%) of benzoyl chloride (b. p. 194-195° at 747 mm, $n^{20}D$ 1.5533).

c) Distillation of 4.9 g (0.019 mole) of benzoyloxytrichlorosilane at atmospheric pressure gave 0.45 g (28%) of silicon tetrachloride (b. p. 56-57°) and 1.7 g (63%) of benzoyl chloride (b.p. 193.5-195° at 747 mm, $n^{20}D$ 1.5535).

## Acylation of Aromatic Hydrocarbons and Thiophene by Benzoyloxytrichlorosilane

The reaction was run in a three neck flask (100 ml) with a stirrer and a reflux condenser with a calcium chloride tube (and a dropping funnel in case of acylation of thiophene).

Benzophenone. a) To the solution of 20 g (0.0785 mole) of benzoxyloxytrichlorosilane in 50 ml of dry benzene there was gradually addedin 3-4 g portions 18 g (0.13 mole) of dry aluminum chloride with the flask being cooled by ice water. Stirring was continued for 15 minutes at 20°, 5 hours at 30-40° and 15-20 minutes on a steam bath. The cooled mass was poured into ice and benzene was steam distilled. Benzophenone was distilled with superheated steam, the distillate was saturated with salt and extracted with ether. The ethereal extract was washed with alkali and water and was dried with anhydrous sodium sulfate. After distillation of the ether there was obtained 10.5 g (73% based on benzoyloxytrichlorosilane or 63.5% based on the benzoic acid taken for the synthesis of benzoyloxytrichlorosilane) of benzophenone with m. p. 45-47°. After distillation (b.p. 142° at 5 mm) benzophenone melted at 47.5-48°, and a sample mixed with an authentic specimen showed no depression.

b) A mixture of 12.2 g of benzoic acid and 29.6 g (0.17 mole) of silicon tetrachloride was heated for 12 hours on a water bath until cessation of evolution of hydrogen chloride. After the distillation of unreacted silicon tetrachloride (9.2 g, i.e., 0.054 mole) there was added to the liquid residue, which was benzoyloxytrichlorosilane, 50 ml of dry benzene followed by 18 g of dry aluminum chloride, as described above. There was obtained 13 g (70% of theoretical amount calculated on benzoic acid) of benzophenone, which after the above-described purification melted at 47.5-48°; a sample of it mixed with authentic benzophenone gave no depression.

4-Methylbenzophenone. To 25.5 g (0.1 mole) of benzoyloxytrichlorosilane there was added 50 ml of toluene; then 18 g of anhydrous aluminum chloride was added gradually as described above. After the appropriate treatment of the reaction mixture, the product was distilled in vacuum. There was obtained 16.05 g (82%) of a fraction with b.p. 140-150° (3 mm) consisting of a mixture of 2-methylbenzophenone with 4-methylbenzophenone. After repeated freezing-out, distillation and recrystallization, there was obtained 8.5 g (53%) of 4-methylbenzophenone with m.p. 57°. Literature data [11]: m.p. 57°.

Found %: C 85.83, 85.77; H 6.29, 6.27. $C_{14}H_{12}O$ Calculated %: C 85.69; H 6.17.

2,4-Dimethylbenzophenone. The synthesis of 2,4-dimethylbenzophenone was conducted as described above: from 25.5 g of benzyloxytrichlorosilane and 50 ml of m-xylene in the presence of 18 g of anhydrous aluminum chloride there was obtained 14.2 g (68%) of 2,4-dimethylbenzophenone:

B.p. 170° (11 mm), $n^{20}D$ 1.5918, $d^{20}_4$ 1.1080. $MR_D$ 64.21. $C_{15}H_{14}O\digamma_6$. Calculated MR 64.58.
Found %: C 85.84, 85.68; H 6.79, 6.94. $C_{15}H_{14}O$. Calculated %: C 85.69; H 6.71.

Literature data [16]: b.p. 320°, $d^{20}_4$ 1.0710.

Benzothienone. To 25.5 g of benzoyloxytrichlorosilane in 50 ml of dry benzene there was added 6.72 g (0.08 mole) of thiophene, after which 10.4 g (0.04 mole) of anhydrous stannic chloride in 20 ml of benzene was added dropwise with stirring. The mixture was heated for three hours on a water bath at 40-60° and for 15 minutes on a steam bath. There was obtained 10.5 g (70%) of benzothienone with m.p. 55-56°; m.p. 56-57° (from alcohol); mixed melting point with authentic benzothienone gave no depression. Literature data: m.p. 56.5-57° [17]; m.p. 55° [18], m.p. 56-57° [6].

### Reaction of Benzoyloxytrichlorosilane With Ethyl Alcohol

a) To a solution of 17.1 g (0.067 mole) of benzoyloxytrichlorosilane in 30 ml of dry benzene cooled to −25° to −30° there was added dropwise 3.1 g (0.067 mole) of anhydrous ethyl alcohol, giving an immediate precipitate of benzoic acid. The mixture was stirred for five hours at 20° (evolution of hydrogen chloride) and the acid was filtered off. There was obtained 5.7 g (69.5%) of benzoic acid with m.p. 121-122°; a mixed specimen with authentic benzoic acid gave no depression.

After distillation of benzene from the filtrate there was obtained on the distillation of the residue a 4.7 g fraction with b.p. 101-120° and a 0.8 g fraction with b.p. 120-130°, in which according to the boiling points there was contained a mixture of ethoxytrichloro- and diethoxydichlorosilanes.

b) Under the same conditions there was obtained, from 25.5 g (0.1 mole) of benzoyloxytrichlorosilane in 30 ml of dry benzene and 13.8 g (0.3 mole) of anhydrous ethyl alcohol, 9.7 g (80%) of benzoic acid with m.p. 121-122°. After distillation of benzene from the filtrate and distillation of the residue there were obtained the following fractions: 1st b.p. 130-156° (740 mm), 2.4 g, and 2nd b.p. 89-90° (70 mm), 8 g.

The first fraction was a mixture of diethoxydichlorosilane and triethoxychlorosilane. The second fraction was tetraethoxysilane (yield 38.5%).

Found %: Si 13.23, 13.31. $C_8H_{20}O_4Si$. Calculated %: Si 13.47.

Literature data: b.p. 165-167° [19], b.p. 60-62° (12 mm) [20].

c) From 25.5 g (0.1 mole) of benzoyloxytrichlorosilane and 18.4 g (0.4 mole) of ethyl alcohol there was obtained 9.4 g of tetraethoxysilane (45%) with b.p. 89-90° (70 mm) and 10.8 g (88%) of benzoic acid with m.p. 121-122°.

## SUMMARY

1. The reaction of benzoic acid with excess silicon tetrachloride yields benzoyloxytrichlorosilane.

2. The formation of benzoyl chloride from benzoic acid and silicon tetrachloride occurs as the result of the reaction of tetrabenzoyloxysilane and benzoyloxytrichlorisilane, the mixture of these being formed in the above reaction, and also as the result of the decomposition of the latter substance at elevated temperature.

3. Benzoyloxytrichlorosilane may be used as an acylating agent for acylation of the benzene nucleus (in the presence of anhydrous aluminum chloride) and for acylation of the thiophene nucleus (in the presence of anhydrous stannic chloride).

4. The benzoyloxy group in benzoyloxytrichlorosilane is more reactive than are the chlorine atoms and is more readily replaced by the ethoxy group during reaction with ethyl alcohol.

## LITERATURE CITED

[1] I. Goubeau and R. Mundiel, Z. anorg u. allg. Chem. 272, 313 (1953).

[2] G. Rauter, Lieb. Ann. 270, 260 (1892).

[3] R. Montonna, J. Am. Chem. Soc. 49, 2114 (1927).

[4] K. A. Andrianov and V. I. Dolgopolov, Ind. Org. Chem. USSR 5, 353 (1938).

[5] Iu. K. Iur'ev, G. B. Eliakov and Z. V. Beliakova, J. Gen. Chem. 24, 1568 (1954).*

[6] Iu. K. Iur'ev and G. B. Eliakov, Doklady Akad. Nauk SSSR 86, 337 (1952); Iu. K. Iur'ev, G. B. Eliakov and Z. V. Beliakova, Bulletin of Moscow State Univ., ser.phys. chem. No. 1, 201 (1956); Iu. K. Iur'ev, Z. V. Beliakova and S. N. Zefirov, J. Gen. Chem. 27, 3264 (1957).*

[7] Iu. K. Iur'ev, G. B. Eliakov and Z. V. Beliakova, Doklady Akad. Nauk SSSR 102, 113 (1955).

[8] Iu. K. Iur'ev, G. B. Eliakov and I. M. Mil'shtein, J. Gen. Chem. 26, 3194 (1956).*

[9] Iu. K. Iur'ev and G. B. Eliakov, Doklady Akad. Nauk SSSR 102, 763 (1955).

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* Original Russian pagination. See C. B. Translation.

[10] Iu. K. Iur'ev, G. B. Eliakov and Z. V. Beliakova, J. Gen. Chem. 26, 2353 (1956).*

[11] K. D. Petrov and E. S. Lagucheva, J. Gen. Chem. 18, 1150 (1948).

[12] K. D. Petrov and M. I. Itkina, J. Gen. Chem. 17, 220 (1947).

[13] K. A. Andrianov, Organosilicon Compounds, State Chem. Press, 143 (1955).**

[14] K. A. Andrianov, A. A. Zhdanov and A. A. Bogdanova, Doklady Akad. Nauk SSSR 94, 697 (1954).

[15] I. Acton and W. Cerrard, Research 8, S 55 (1955).

[16] A. Klages, Ber. 32, 1565 (1899).

[17] H. Hartough, A. Kosak and I. Sardella, J. Am. Chem.Soc. 69, 1014 (1947).

[18] A. Comey, Ber. 17, 790 (1884).

[19] A. Dearing and E. Reid, J. Am. Chem. Soc. 50, 3059 (1928).

[20] B. Helferich and I. Hausen, Ber. 57, 796 (1924).

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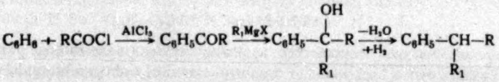
*Original Russian pagination. See C. B. Translation.

**In Russian.

# SYNTHESIS OF UNDECYL AND DODECYLBENZENES AND THEIR PERHYDRIDES

A. D. Petrov, G. I. Nikishin and V. D. Vorob'ev

The first individual dodecylbenzene (3-methyl-1-phenylundecane) was synthesized for the purpose of studying the optical activity of its perhydrides [1]. Other isomers of it, as well as alkylbenzenes with lower molecular weights, were obtained in view of the interest they presented as hydrocarbon models of diesel fuels. In recent years the interest in dodecylbenzenes has increased considerably among investigators studying the effects of alkylbenzene structure on the wetting properties of sodium alkylbenzenesulfonates. Out of 3059 possible isomers of dodecylbenzene [2] only fourteen have been synthesized till now. Six of them (isomers with normal hydrocarbon chain and varying locations of the phenyl ring) were synthesized according to this scheme [3-5]:



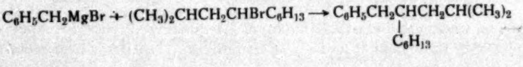
$$C_6H_6 + RCOCl \xrightarrow{AlCl_3} C_6H_5COR \xrightarrow{R_1MgX} C_6H_5-\underset{R_1}{\overset{OH}{C}}-R \xrightarrow[+H_2]{-H_2O} C_6H_5-\underset{R_1}{CH}-R$$

We prepared 2-phenyldodecane through alkylation of benzene with dodecyl alcohol [6] or with dodecane-1 [7]; 1-phenyldodecane was obtained by Clemmensen [8] or Kishner [9] reduction of laurylphenone. The acylation step in the above described scheme can be replaced with oxidation of a corresponding alcohol to ketone [10]. Alkylbenzenes with quaternary carbon atoms next to the benzene were made by alkylating the latter with tertiary halides [11] or (as in the case of 2-methyl-2-phenylundecane, 4-methyl-4-phenylundecane, and 6-methyl-6-phenylundecane) with olefins possessing a double bond next to the tertiary carbon atom [12]. A series of isomers: previously mentioned 3-methyl-1-phenylundecane [1], 4-butyl-1-phenyloctane [13], 6-methyl-1-phenylundecane [14], and 2,8-dimethyl-5-benzylnonane [15] were synthesized in several steps using either Friedel-Crafts or Grignard reactions.

It is evident from this description that dodecylbenzenes with branched alkyl chains (i.e., hydrocarbon models of technical dodecylbenzene) have not yet been sufficiently studied. We synthesized hydrocarbons of composition $C_{17}$ and $C_{18}$ through the following reactions:

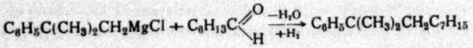
a) 1-Phenylalkane type

1. $C_6H_5CH_2CH_2COOC_2H_5 + 2C_4H_9MgBr \xrightarrow[+H_2]{-H_2O} C_6H_5CH_2CH_2CH(C_4H_9)_2$

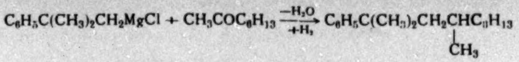
2. 

$$C_6H_5CH_2MgBr + (CH_3)_2CHCH_2CHBrC_6H_{13} \rightarrow C_6H_5CH_2\underset{C_6H_{13}}{CH}CH_2CH(CH_3)_2$$

b) 2-Phenylalkane type (two of them with quaternary carbon atoms next to the benzene ring)

3. 

$$C_6H_5C(CH_3)_2CH_2MgCl + C_6H_{13}C\overset{O}{\underset{H}{\lessgtr}} \xrightarrow[+H_2]{-H_2O} C_6H_5C(CH_3)_2CH_2C_7H_{15}$$

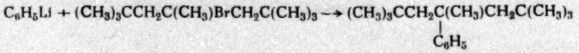
4. 

$$C_6H_5C(CH_3)_2CH_2MgCl + CH_3COC_6H_{13} \xrightarrow[+H_2]{-H_2O} C_6H_5C(CH_3)_2CH_2\underset{\substack{|\\ CH_3}}{C}HC_6H_{13}$$

5. $C_6H_5COCH_3 + (CH_3)_2C{=}CHCH_2CH_2CH(CH_3)CH_2CH_2MgBr \xrightarrow[+H_2]{-H_2O}$

$\longrightarrow C_6H_5CH(CH_3)CH_2CH_2CH(CH_3)CH_2CH_2CH_2CH(CH_3)_2$

And finally, we obtained a dodecylbenzene with maximum branching in the alkyl chain.

6. 

$$C_6H_5Li + (CH_3)_3CCH_2C(CH_3)BrCH_2C(CH_3)_3 \longrightarrow (CH_3)_3CCH_2\underset{\substack{|\\ C_6H_5}}{C}(CH_3)CH_2C(CH_3)_3$$

The choice of these forms was dictated by the desire to find out whether highly or slightly branched homologs of technical dodecylbenzenes are preferable for the manufacture of wetting compounds. We determined solidification points and kinematic viscosities at 20 and 50° of all the hydrocarbons obtained by reactions 1-5. These data are listed in the Table, and n-dodecylbenzene (synthesized by Schmidt and co-workers [9]) is given for comparison. The solidification points of alkylbenzenes (in the 80-90° range) are on the average 5° lower than those of corresponding alkylcyclohexanes. One can see from the Table that the effect of hydrocarbon structure on the magnitude of kinematic viscosity at + 20°, and especially at + 50° is not very pronounced. At temperatures below zero the effect becomes much more apparent. Thus for hydrocarbon (VIII) $\nu_0$ 17.64, $\nu_{-20}$ 67.46, $\nu_{-40}$ 393.44; for (IX) $\nu_0$ 24.40, $\nu_{20}$ 105.70, $\nu_{40}$ 901.20.

## EXPERIMENTAL

2,2,4,6,6-Pentamethyl-4-phenylheptane (II). a) Triisobutylene (made through polymerization of isobutylene in sulfuric acid) was treated over a long period of time with excess of hydrogen bromide at room temperature. Addition of hydrogen bromide was very slow. Vacuum distillation yielded a bromide, b.p. 99-101° (12 mm), $n^{20}D$ 1.4710, $d^{20}_4$ 1.0572, which evidently had the 2,2,4,6,6-pentamethyl-4-bromopentane structure.

b) The whole dodecylbromide (30.5 g, 0.12 moles) was poured directly into an ether solution of phenyllithium; phenyllithium was made from 5.1 g (0.73 g-at.) of lithium and 57 g (0.36 moles) of bromobenzene, then separated from unreacted lithium. The reaction mixture was boiled for 3 hours, then part of the ether was distilled off, and heating was continued for 6 more hours at 70°. We isolated from the reaction mixture 10 g (30%) of dodecylbenzene in the normal way; its properties are listed in the Table. The structure ascribed to this hydrocarbon is based only on the fact that 90% of triisobutylene (prepared from isobutylene with sulfuric acid) is composed of two isomers: 1,1-dineopenthylethylene and 2,2,4,6,6-pentamethylheptene-3 [16].

2,4-Dimethyl-2-phenyldecane (III). a) An ether solution of a Grignard reagent was prepared from 337 g (2 moles) of 1-chloro-2-methyl-2-phenylpropane and 73 g (3 g-at.) of magnesium; to this solution we added 197 g (1.5 moles) of methylhexylketone. (We prepared 1-chloro-2-methyl-2-phenylpropane in a 78% yield through alkylation of benzene with methallyl chloride in sulfuric acid.) After boiling for 6 hours we decomposed the reaction mixture with water and 5% hydrochloric acid. We isolated 235 g (60%) of 2,4-dimethyl-2-phenyldecanol-4 from its ether solution.

B.p. 143-144° (2.5 mm), $n^{20}D$ 1.4918, $d^{20}_4$ 0.9064, $MR_D$ 83.87; calc. 83.75.
Found %: C 82.26; H 11.49. $C_{18}H_{30}O$. Calculated %: C 82.38; H 11.52.

b) A mixture containing 100 g (0.25 moles) of 2,4-dimethyl-2-phenyldecanol-4 and 178 g of 60% sulfuric acid was refluxed until the organic layer became transparent. Distillation over metallic sodium yielded 66 g (71%) of 2,4-dimethyl-2-phenyldecene.

B.p. 129-130° (2 mm), $n^{20}D$ 1.4950, $d^{20}_4$ 0.8756, $MR_D$ 81.38; calc. 81.85.

c) We hydrogenated 60 g of 2,4-dimethyl-2-phenyldecene at 120 atm in an autoclave over Raney nickel (10 g). The 2,4-dimethyl-2-phenyldecane (properties listed in the Table) obtained did not decolorize an alcoholic solution of bromine.

*5,9-Dimethyl-2-phenyldecane (IV).* a) We prepared 164.5 g (0.75 moles) of 3,7-dimethyl-1-bromooctene-6 from citronellol and phosphorus tribromide and added it slowly to 30.5 g (1.2 g-at.) of magnesium placed in ether. We added to the Grignard reagent 120 g (1 mole) of acetophenone over a period of 4 hours, then refluxed the reaction mixture for 10 hours. We decomposed the reaction mixture with water and vacuum distilled the ether solution; we isolated 120 g (66%) of 5,9-dimethyl-2-phenyldecadiene (dehydration product of a tertiary alcohol).

B.p. 162-164° (4 mm), $n^{20}D$ 1.5125, $d^{20}_4$ 0.8843, $MR_D$ 82.66; calc. 81.27.
Found %: C 88.43; H 10.97. $C_{18}H_{26}$. Calculated %: C 88.86; H 11.14.

b) We hydrogenated 76 g of 5,9-dimethyl-2-phenyldecadiene (mixed with 120 g of methyl alcohol) over Raney nickel (15 g) at 40° and 125 atm. The properties of 5,9-dimethyl-2-phenyldecane are listed in the Table.

*2-Methyl-4-hexyl-5-phenylpentane (V).* Benzene magnesium chloride was prepared from 185 g (1.4 moles) of chlorobenzene and 48 g (2 g-at.) of magnesium in ether. After removal of unreacted magnesium, 166 g (0.7 moles) of 2-methyl-4-bromodecane was added all at once to the organomagnesium compound at room temperature. No visible signs of reaction were observed. Most of the ether was distilled off, and the contents of the flask heated for 6 hours at 90-100°; after this, the ether which was previously distilled off was poured back into the flask and the reaction mixture decomposed with water. We isolated 116 g (67%) of 2-methyl-4-hexyl-5-phenylpentane from the ether solutions.

*2-Methyl-4-phenyldecane (VI).* a) We added 167 g (1.5 moles) of heptanol to an organomagnesium compound prepared from 200 g (1.2 moles) of 1-chloro-2-methyl-2-phenylpropane and 48.6 g (2 g-at.) of magnesium. We isolated 180 g (60%) of 2-methyl-2-phenyldecanol-4 from the reaction mixture in the usual way.

B.p. 149-150° (2 mm), $n^{20}D$ 1.5003, $d^{20}_4$ 0.9281, $MR_D$ 78.65, calc. 79.10.
Found %: C 82.90; H 11.30. $C_{17}H_{28}O$. Calculated %: C 82.19; H 11.36.

b) We boiled 145 g of 2-methyl-2-phenyldecanol-4 for 15 hours in 217 g of 60% $H_2SO_4$. We obtained 109 g (81%) of 2-methyl-2-phenyldecene.

B. p. 136-137° (5.5 mm), $n^{20}D$ 1.4982, $d^{20}_4$ 0.8740, $MR_D$ 77.20; calc. 77.10.
Found %: C 88.70; H 11.30. $C_{17}H_{26}$. Calculated %: C 88.63; H 11.37.

c) We mixed 105 g of 2-methyl-2-phenyldecene with 140 g of methyl alcohol and hydrogenated over 20 g of Raney nickel in a liter autoclave. The initial pressure was 132 atm, temperature 20°. The 2-methyl-2-phenyldecane previously obtained [17] from bromooctane and phenylisopropyl potassium had the following properties: $n^{20}D$ 1.4859, $d^{20}_4$ 0.8676, b.p. 160° (20 mm).

*3-Butyl-1-phenylheptane (VII).* To an ether solution of butylmagnesium bromide (made from 274 g (2 moles) of butyl bromide and 62 g (2.5 g-at.) of magnesium) slowly we added 134 g (0.75 moles) of ethyl hydrocinnamate. The reaction mixture was boiled for 6 hours and decomposed with water. We isolated 146 g (78.5%) of 3-butyl-1-phenylpentanol-3 from its ether solution.

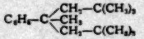
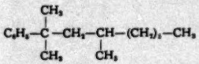
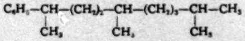
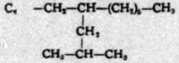
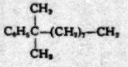
B.p. 140-142° (3 mm), $n^{20}D$ 1.5000, $d^{20}_4$ 0.9261, $MR_D$ 78.89; calc. 79.10.
Found %: C 82.20; H 11.40. $C_7H_{28}O$. Calculated %: C 82.19; H 11.36.

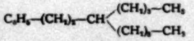
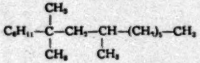
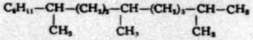
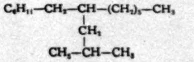
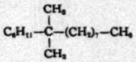
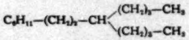
b) We boiled 126 g of 3-butyl-1-phenylheptanol-3 for 3 hours with 200 g of 60% sulfuric acid. As a result we obtained 108 g (92.5%) of 3-butyl-1-phenylheptene.

B.p. 116-118° (2 mm), $n^{20}D$ 1.4980, $d^{20}_4$ 0.8793, $MR_D$ 76.77; calc. 77.10.
Found %: C 87.98; H 11.26. $C_{17}H_{26}$. Calculated %: C 88.63; H 11.37.

c) We hydrogenated 98 g of 3-butyl-1-phenylheptene in a liter autoclave over 15 g of Raney nickel; the initial pressure was 120 atm, temperature 50°. The properties of the alkylbenzene obtained are listed in the Table.

*Hydrogenation of dodecyl and undecylbenzenes (II-V).* Hydrogenation was carried over Raney nickel at 180-200° under a 200-220 atm pressure. To ascertain the purity of dodecyl and undecylcyclohexanes obtained, we took ultraviolet spectrum of hydrogenated 2-methyl-2-phenyldecane and were unable to detect the characteristic benzene lines.

| Substances | Compound | Boiling point (pressure in mm) | Solidification point | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ |  |  | Viscosity (in centistokes) |  | Found* |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  | calc. from |  | found |  |  |  |  |
|  |  |  |  |  |  | atoms | comp. |  | 20° | 50° | % C | % H |
| (I) | $C_6H_5-CH_2-(CH_2)_{10}-CH_3$[*]<br>Dodecylbenzene | 183—185° (12) | — | 1.4822 | 0.8364 | 81.72 | 82.23 | 82.06 | 6.294 | 3.191 | — | — |
| (II) |  $C_6H_5-C\begin{matrix}\diagup CH_2-C(CH_3)_3\\ -CH_3\\ \diagdown CH_2-C(CH_3)_3\end{matrix}$<br>2,2,3,6,6-Pentamethyl-4-phenylheptane | 133—135 (14) | — | 1.4930 | 0.8811 | 81.72 | 82.23 | 81.28 | — | — | 88.10, 88.00 | 12.10, 12.10 |
| (III) |  $C_6H_5-\underset{CH_3}{\overset{CH_3}{\overset{\vert}{\underset{\vert}{C}}}}-CH_2-\underset{CH_3}{\underset{\vert}{CH}}-(CH_2)_5-CH_3$<br>2,4-Dimethyl-2-phenyldecane | 136—136.5 (5) | —89 ст | 1.4850 | 0.8637 | 81.72 | 82.23 | 81.74 | 6.896 | 3.288 | 87.52, 87.74 | 12.40, 12.41 |
| (IV) |  $C_6H_5-\underset{CH_3}{\underset{\vert}{CH}}-(CH_2)_2-\underset{CH_3}{\underset{\vert}{CH}}-(CH_2)_3-\underset{CH_3}{\underset{\vert}{CH}}-CH_3$<br>5,9-Dimethyl-2-phenyldecane | 134—135 (2) | —82 ст | 1.4815 | 0.8553 | 81.72 | 82.23 | 82.05 | 8.012 | 3.533 | 87.64, 87.60 | 12.38, 12.29 |
| (V) |  $C_6\ -CH_2-\underset{CH_3-\underset{\vert}{CH}-CH_3}{\underset{\vert}{\underset{CH_2}{\underset{\vert}{CH}}}}-(CH_2)_5-CH_3$<br>2-Methyl-4-hexyl-5-phenylpentane | 130.5 (3) | —81 ст | 1.4889 | 0.8657 | 81.72 | 82.23 | 82.14 | 6.794 | 3.007 | 88.07, 87.92 | 11.80, 11.80 |
| (VI) |  $C_6H_5\underset{CH_3}{\overset{CH_3}{\overset{\vert}{\underset{\vert}{C}}}}-(CH_2)_7-CH_3$<br>2-Methyl-2-phenyldecane | 146.5 (2) | —93 ст | 1.4881 | 0.8665 | 77.11 | 77.58 | 77.28 | 6.528 | 3.015 | 87.96, 87.75 | 12.06, 11.98 |

|  |  |  |  |  |  |  |  |  |  |  |  |
|---|---|---|---|---|---|---|---|---|---|---|---|
| (VII) |  $C_6H_5-(CH_2)_2-CH\left\langle\begin{matrix}(CH_2)_3-CH_3\\(CH_2)_3-CH_3\end{matrix}\right.$<br>3-Butyl-1-phenylheptane | 134 (3) | −97 ст | 1.4839 | 0.8569 | 77.11 | 77.58 | 77.58 | 5.160 | 2.450 | 87.62, 87.75 | 12.23, 12.12 |
| (VIII) |  $C_6H_{11}-\underset{CH_3}{\overset{CH_3}{C}}-CH_2-\underset{CH_3}{CH}-(CH_2)_5-CH_3$<br>2,4-Dimethyl-2-cyclohexyldecane | 134—135 (2) | −83 ст | 1.4778 | 0.8546 | 83.12 | 83.51 | 83.60 | 7.551 | 3.627 | — | — |
| (IX) |  $C_6H_{11}-\underset{CH_3}{CH}-(CH_2)_2-\underset{CH_3}{CH}-(CH_2)_3-\underset{CH_3}{CH}-CH_3$<br>5,9-Dimethyl-2-cyclohexyldecane | 140—141 (3) | −79 ст | 1.4698 | 0.8442 | 83.12 | 83.51 | 83.41 | 8.776 | 3.701 | — | — |
| (X) |  $C_6H_{11}-CH_2-\underset{\substack{CH_2\\CH_3-CH-CH_3}}{CH}-(CH_2)_5-CH_3$<br>2-Methyl-4-hexyl-5-cyclohexylpentane | 138—139 (5) | −75 ст | 1.4659 | 0.8375 | 83.12 | 83.51 | 83.47 | 9.126 | 3.779 | — | — |
| (XI) |  $C_6H_{11}-\underset{CH_3}{\overset{CH_3}{C}}-(CH_2)_7-CH_3$<br>2-Methyl-2-cyclohexyldecane | 124—125 (2) | −86 ст | 1.4764 | 0.8540 | 78.50 | 78.86 | 78.81 | 7.493 | 3.297 | — | — |
| (XII) |  $C_6H_{11}-(CH_2)_2-CH\left\langle\begin{matrix}(CH_2)_3-CH_3\\(CH_2)_3-CH_3\end{matrix}\right.$<br>3-Butyl-1-cyclohexylheptane | 134—135 (4) | −92 ст | 1.4570 | 0.8252 | 78.50 | 78.86 | 78.67 | 9.360 | 3.870 | — | — |

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* Substances (II–V) $C_{18}H_{30}$. Calculated %: C 87.72; H 12.28. Substances (VI–VII) $C_{17}H_{28}$. Calculated %: C 87.87; H 12.13.

## SUMMARY

A series of undecyl, dodecylbenzenes and their perhydrides was synthesized. Kinematic viscosities and solidification points were determined for the synthesized hydrocarbons.

## LITERATURE CITED

[1] P. A. Levene and S. A. Harris, J. Biol. Chem. 3, 735 (1935).

[2] B. F. Pishnamazzade, Bull. Acad. Sci. Azerb. SSR, No. 1, 35 (1957).

[3] A. W. Schmidt, and A. Grosser, Ber. 75, 829 (1942).

[4] H. Gilman and R. N. Meals, J. Org. Ch. 8, 126 (1943).

[5] T. Asahara and I. Takagi, J. Chem. Soc. Japan, Ind. Chem. Soc. 58, 147 (1955).

[6] N. F. Toussaint and G. F. Hennion, J. Am. Chem. Soc. 62, 1145 (1940).

[7] W. Z. Zennemann, R. Hites, and V. I. Komarewsky, J. Org. Ch. 19, 463 (1954).

[8] A. D. Petrov, and E. I. Lapteva, J. Gen. Chem. 7, 205 (1937); R. Paquette, E. Zinguffelter and H. Tartar, J. Am. Chem. Soc. 65, 685 (1943); W. Griess, Fette, Seifen, Austrichmittel 57, 236 (1955).

[9] F. W. Gray, I. F. Gerecht and I. J. Krems, J. Org. Ch. 20, 511 (1955); A. W. Schmidt, G. Hopp and V. Schoeller, Ber. 72, 1893 (1939).

[10] A. D. Petrov, E. I. Lapteva and A. N. Pchelkina, J. Gen. Chem. 14, 495 (1944).

[11] O. M. Halse, J. pr. Ch. 89, 451 (1914).

[12] P. L. Kooljman, H. W. Huliser and I. L. Tsepkema, I. Congres mondial de la dotergence et des produits tensio actifs, T. I. 130 (1954).

[13] W. Griess, Fette, Seifen, Austrichmittel, 57, 236 (1955).

[14] W. E. Truce and I. Twise, J. Am. Chem. Soc. 72, 2300 (1950).

[15] I. Braun and O. Schittnez, Ber. 74, 24 (1941).

[16] F. C. Whitmore, C. D. Wilson and I. V. Capinjolo et al., J. Am. Chem. Soc. 63, 2035 (1941).

[17] K. Zigler, H. Grimm and R. Willer, Lieb. Ann., 542, 90 (1939).

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# RESEARCH IN THE FIELD OF SYNTHESIS AND CONDENSATION OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE

## V. REACTION MECHANISM OF REDUCTIVE ALKYLATION OF HEXAMETHYLENEDIAMINE

A. L. Klebanskii and M. S. Vilesova

In order to clarify the reaction mechanism of reductive alkylation of hexamethylenediamine, it was necessary to consider the problem of possible intermediate products and the role of catalyst.

It is generally accepted that an azomethine base (Schiff's base) is formed as an intermediate in the reductive alkylation [1]. In order to find out if a Schiff's base was present as an intermediate product, we compared the reduction rate of a hexamethylenediamine–butyraldehyde mixture with that of a corresponding azomethine base:

$$CH_3CH_2CH_2CH=N(CH_2)_6N=CHCH_2CH_2CH_3$$

both rates were measured in an alcoholic solution. In Fig. 1 we showed that the reduction of the above mentioned mixture proceeds much faster than that of pure Schiff's base. Since the slowest stage determines the over-all reaction rate, it is obvious that an azomethine base could not be an intermediate product in the reductive alkylation.

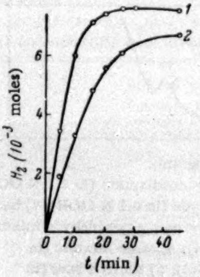
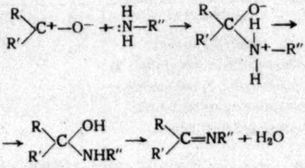


Fig. 1. Reduction of hexamethylenediamine–butyraldehyde mixture (Curve 1), and of a corresponding Schiff's base (Curve 2) under atmospheric pressure.

In connection with the question brought up above another one arose: what adducts could be present in a hexamethylenediamine–carbonyl compound mixture before reduction takes place? In accordance with the usual electronic representation [2], the interaction of an aldehyde or ketone with an amine can be illustrated by the following scheme:



According to this scheme we would expect that besides starting materials, hydroxyl containing products and Schiff's bases would be present in the reaction mixture. Since, as the kinetic data would indicate, Schiff's base could not be an intermediate (but if it was, it would not be the only intermediate to determine the whole reaction rate), a doubt arose if it was formed at all under mild conditions; maybe the hydroxyl compound is an intermediate and is catalytically reduced.

To answer this question, we obtained some infrared spectra of starting materials, of their mixture, and of a corresponding Schiff's base (Fig. 2) in the 1400-1800 $cm^{-1}$ regions (an IKS-11 spectrometer with a rock salt

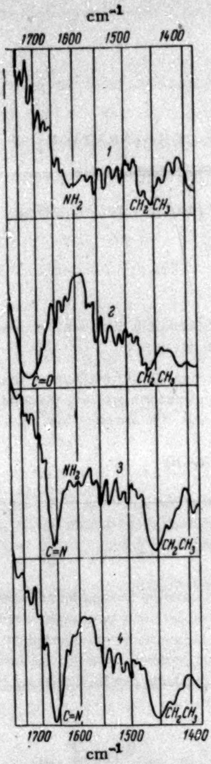


Fig. 2. Infrared spectra.
1) Hexamethylenediamine; 2) butyraldehyde; 3) hexamethylenediamine–butyraldehyde mixture; 4) Schiff's base.

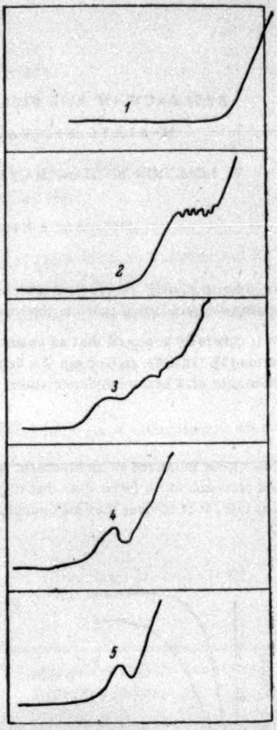


Fig. 3. Polarograms.
1) Hexamethylenediamine (in 0.1 N LiOH); 2) butyraldehyde (in 0.1 N LiOH); 3) hexamethylenediamine–butyraldehyde mixture (in 0.1 N LiOH); 4) same mixture (in absolute alcohol); 5) Schiff's base (in absolute alcohol).

prism was used). The spectra of initial diamine and butyraldehyde show vibrational absorption bands corresponding to the $NH_2$ and $C=O$ bonds respectively. A very intense band was observed at a frequency of 1668 $cm^{-1}$; this band corresponds to the $C=N$ bond vibration and was absent in the starting material. The same frequency was observed in the spectrum of Schiff's base. The mixtures also showed a very intense absorption in the region corresponding to a OH bond vibration (3500-3700 $cm^{-1}$). However, it was hard to decide whether it was due to the presence of $H_2O$ (water is split out when Schiff's base is formed), or the presence of hydroxyl-containing compounds formed as a result of diamine addition to the aldehyde. Spectra of acetone and its mixture with hexamethylenediamine were also obtained; these fully matched the spectra obtained for butyraldehyde and its mixture with the same amine.

The above mentioned spectroscopic data* would indicate that in a diamine–carbonyl compound mixture a Schiff's base is rapidly formed. We were not able to detect any hydroxyl-containing intermediates by comparing the spectrum with that of a compound approximately resembling it structurally: $R-CHOH-CH_2-NHCH_3$.

A hydroxyl intermediate ($R'R''COH-NH-(CH_2)_6-NH-COHR'R''$) must exist in the formation of an azomethine base; however, it evidently is unstable (because of two functional groups on one carbon) and is immediately converted into a Schiff's base as soon as it is formed. Hence, for the reason just stated, there is no ground to consider it an intermediate in solution.

A supplementary polarographic study of individual compounds and their mixtures carried in solution** confirmed the spectroscopic data qualitatively (spectra were made without solvents). One can see on the polarograms (Fig. 3, Curve 1), that hexamethylenediamine is not reduced on a mercury-drop electrode and its polarogram looks straight. Butyraldehyde gives a strong reduction wave (Fig. 3, Curve 2). The diamine–aldehyde mixture gives two waves; the first one corresponds to the newly formed compound, the second one to the remaining unreacted butyraldehyde (Curve 3). The polarogram of Schiff's base has a reduction wave which is identical with the one found in the mixture, and which is due to the $C=N$ linkage (Curve 4). The data obtained showed that besides remaining free starting materials, a Schiff's base is also formed when a diamine–carbonyl compound mixture is dissolved in alcohol. The formation of a Schiff's base in a solution containing a mixture of diamine and carbonyl compound is not a sufficient basis for considering it the primary intermediate product in the reductive alkylation, for this idea would be inconsistent with the kinetic data on the reduction rate of the mixture and of a corresponding Schiff's base.

One could assume that if starting materials are chemisorbed much faster on the catalyst then are Schiff's bases, then this would constitute a decisive factor in making the catalytic reduction rate of the mixture greater than that of the corresponding azomethine base.

We set up experiments whereby azomethine bases and corresponding diamine–aldehyde mixtures could be reduced with atomic hydrogen (nascent) without utilizing a catalyst; this would exclude any effects which a catalytic absorption of reaction constituents might have on the course of reductive alkylation. Two variations of the experiment were used: with Na in ethanol, or with Zn in dilute HCl; the data on the reduction rates (based on the determination of the number of unsubstituted amino groups) are listed in the Table, and it is evident that in this case the Schiff's base was hydrogenated much faster than the mixture (in contrast to the catalyzed process). The reaction rate depends on the concentration of Schiff's base, and in the case of the mixture it should be determined by the rate at which $C=N$ bonds are formed. The experiments in which reduction was done by nascent hydrogen indicate also, that the concentration of Schiff's base as a diamine–aldehyde mixture is not large under these conditions (dilute solutions, acidic or alkaline medium).

Reduction of Hexamethylenediamine–Butyraldehyde Mixture and a Corresponding Schiff's Base With Nascent Hydrogen

| The substance reduced | Conditions of reduction | The amount of product that reacted after 3 hrs. (in %) |
|---|---|---|
| Schiff's base | Zn + HCl | 87 |
| Mixture | Zn + HCl | 9 |
| Schiff's base | Na + $C_2H_5OH$ | 91 |
| Mixture | Na + $C_2H_5OH$ | 10 |

Thus, on the basis of the cited experimental material one can assume that a diamine–carbonyl compound mixture contains not only the starting materials but also a small concentration of nascent Schiff's base (under catalytic reduction conditions). Kinetic experiments give no grounds for the assumption that the reaction proceeds through a stage at which Schiff's base is adsorbed from solution. The rate determining step in the reductive alkylation is the chemisorption of individual starting components (diamine and aldehyde or ketone) and subsequent interaction on closer approach on the active surface. In such a case the faster adsorption of the components will make the reduction rate of the mixture greater; the adsorption rate depends on polarizability, and Schiff's bases (which may be formed on the active surface) are much less polarizable than compounds with $NH_2$ and CO groups.

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*Spectra were determined by L. D. Shcherba.

**Polarograms were determined by L. P. Seliutina.

## EXPERIMENTAL

1. Synthesis of an azomethine base. The reaction was conducted in a round-bottomed three-necked flask which was supplied with a mechanical stirrer, a thermometer, and a dropping funnel. We placed 58 g of hexamethylenediamine and added 76 g of butyraldehyde dropwise (flask was cooled with ice). We added 20 g of fused KOH to the reaction mixture. The reaction lasted 2 hours. At first the reaction warmed up to 75°, then it continued at room temperature. When it was terminated, we distilled off unreacted aldehyde, dissolved the mixture in 400 ml of ether, washed away unreacted diamine with water, and dried over $K_2CO_3$. After removal of ether, the residue was fractionally distilled under reduced nitrogen pressure. A constant boiling fraction, b.p. 119-121° (3 mm), was collected; it was a Schiff's base made of hexamethylenediamine and butyraldehyde.* We obtained 28 g (25%) of azomethine.

B.p. 119-121° at 3 mm, $d^{25}_4$ 0.836, $n^{25}D$ 1.4539, $MR_D$ 72.4; calc. 72.2.
Found %: N 12.5 (by Kjeldahl method); C=N 22.27 (by hydrogenation according to Willstätter). M 240 (method of Rast). $C_{14}H_{30}N_2F_2$. Calculated %: N 12.37; C=N 22.96. M 226.4.

Under the conditions of the Van Slyke determination of $NH_2$ content, Schiff's base is unstable and decomposes into a diamine and aldehyde.

2. Catalytic reduction of a hexamethylenediamine–butyraldehyde mixture, and of a corresponding Schiff's base. Experiments were conducted in a Willstätter duck-shaped apparatus under atmospheric pressure (method described in [3]). We used in this reduction 0.460 g of hexamethylenediamine in 23.8 ml of alcohol and 0.571 g of n-butyraldehyde (a 1 : 2 molar ratio). For the hydrogenation of Schiff's base we took 0.896 g of it in 23.9 ml of alcohol. The volume of mixture was 25 ml, the quantity of platinum oxide 0.1000 g, and the concentration of diamine or Schiff's base 0.160 moles/liter; these amounts were kept constant in both cases. The data on the absorption rate of hydrogen are shown in Fig. 1. Results were the same when experiments were carried out with double the concentration of diamine and Schiff's base.

3. Reduction of a hexamethylenediamine–butyraldehyde mixture, and of a corresponding Schiff's base using atomic hydrogen. The reaction was carried out in a two-necked flask supplied with a reflux condenser, a dropping funnel, and a stirrer; the temperature was kept 20 ± 0.1° in a thermostat. We placed an alcoholic or aqueous solution of hexamethylenediamine together with pieces of sodium or zinc powder in the flask; to this we added alcohol or hydrochloric acid (1 : 1), and as soon as hydrogen evolution began we turned the stirrer on and added (through a dropping funnel) a weighed portion of butyraldehyde or Schiff's base. The funnel was then rinsed out with whatever solvent was used in reaction. After 3 hours we stopped the reaction, separated the reaction mixture from residues, measured its volume, and analyzed for $NH_2$ groups. The number of substituted $NH_2$ groups was used as a control for this analysis.

We used 0.891 g of hexamethylenediamine and 1.108 g of butyraldehyde or 1.719 g of Schiff's base respectively. The quantity of solvent was 97 ml of ethyl alcohol or hydrochloric acid (1 : 1) for the mixture, and 98 ml of the same ones for hydrogenation of Schiff's base. In all the cases the volume of the reaction mixture was 100 ml. We used 10.0 g of sodium and 15.0 g of zinc powder. The concentration of diamine or Schiff's base was kept at $77 \times 10^{-3}$ moles/liter in all the experiments. The experimental results are shown in the Table.

## SUMMARY

1. The presence of Schiff's base in a hexamethylenediamine–butyraldehyde mixture was established with the help of infrared spectra and polarography.

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* This compound has been obtained and characterized for the first time.

2. We established that the catalytic hydrogenation rate is greater for the diamine–aldehyde mixture than for a corresponding Schiff's base.

3. We showed that if hydrogenation is done with nascent hydrogen, then the reduction rate of Schiff's base is much greater than that of a hexamethylenediamine–carbonyl compound mixture.

4. A mechanism is offered for the reductive alkylation; according to it, the diamine and the carbonyl compound are chemisorbed individually on the catalyst, interact, and are reduced in the adsorbed state. The chemisorption rate of individual constituents will determine the rate of reductive alkylation. The reduction of the Schiff's base present in solution does not completely determine the course of reaction.

## LITERATURE CITED

[1] Org. Reacts. Coll. 5, 347 (1951).*

[2] A. I. Kiprianov, Electronic Theory in Organic Chemistry, Izd. AN Ukrainian USSR, 94 (1949).*

[3] A. L. Klebanskii and M. S. Vilesova, J. Gen. Chem. 28, 1066 (1958).**

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*In Russian.

**Original Russian pagination. See C. B. Translation.

# RESEARCH IN THE FIELD OF SYNTHESIS AND CONDENSATION OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE

## VI. SYNTHESIS OF POLYAMINES STARTING WITH N-ALKYLATED HEXAMETHYLENEDIAMINE. PRODUCTION OF PARTLY N-ALKYLATED POLYAMIDES

A. L. Klebanskii and M. S. Vilesova

Fundamental properties of polyamides (crystallinity, tensile strength, stability in organic solvents et al.) indicate characteristically strong intermolecular interactions which are due to van der Waals forces and hydrogen bonding [1]. Due to the strong additive character of these linkages (whose total energy may exceed that of C–C bonds [2]) the intermolecular interaction among polyamides is consequently much greater than among a series of other synthetic polymers [3].

Briggs, Frosch, and Erickson [4] investigated the effect of the degree and regularity of N-methylation on the melting points of substituted polyamides; they connected their data with the degree of crystallinity in the polymer. Wittbecker et al. [5] have investigated a series of substituent radicals, and showed that an isobutyl-substituted polyamide of definite composition and with dispersed substituents constituted a substance with increased elasticity; some properties (determined in experiments conducted on threads) are close to those of synthetic rubber.

In order to disrupt the crystalline structure of polyamides and give them elastic properties, we obtained in this work a series of products, by starting with variously substituted (with respect to N or N') diamines and mixing them with unsubstituted diamines. When N,N'-disubstituted diamines are used in polycondensation, they form polyamides without intermolecular hydrogen bonds and with substantially weakened van der Waals interactions (which stipulates an balsam-like consistency in polycondensates); to these diamines we applied a special after-treatment with diisocyanates which leads to the formation of comparatively sparsely distributed bridged valence bonds. In this manner, two principally different types of polyamides were obtained. In the first one of these, polycondensation results in relatively short polymeric molecules, which are linked to each other through hydrogen bonds. The polymers of the second type are characterized by a complete absence of hydrogen bonding and by a lengthening of main polyamide chains; the lengthening is due to the reaction of end groups with diisocyanate and the presence of bridged valence bonds between chains (these are formed when diisocyanate reacts with carbamide groups formed on chain lengthening). These polymers are characterized by a straight chain structure; the properties can vary depending on the structure of substituents (size, branching), length of initial chain section, and finally, on the structure of the diisocyanate molecules themselves. Thus, the polymers of the second type present more possibilities for a guided modification of their chemical and physicomechanical properties (for the synthesis of this type of polymers see communication VII).

The synthesis of partially N-alkylated polyamides was accomplished through copolymerization of N,N'-di, N-monosubstituted, and unsubstituted adipamides in different proportions.

For the polycondensation with adipic acid (to obtain a partially N-substituted polyamide) we used N,N'-diisoprophylhexamethylenediamine and N-monoisopropylhexamethylenediamine out of a whole series of N-substituted diamines synthesized in this work. The choice of just these was determined for the following considerations: in the first place, the isopropyl group, having destroyed the hydrogen bond by replacing a hydrogen on the nitrogen, decreases the possibility of secondary phenomena (due to high branching and relatively short chain length) connected

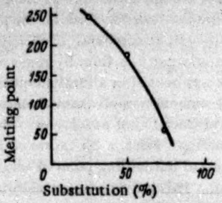

Fig. 1. Melting points of polyamides as a function of the degree of N-alkylation (as an example N-isopropyl substituted).

with orientation of a long substituent chain alongside the polymer chain [5], and with interaction of substituents themselves; in the second place, the synthesis of initial monomeric N-isopropylhexamethylenediamine derivatives proceeds smoothly with optimum yields and reaction rates, and also requires such a readily available product as acetone for alkylation.

Adipamides of the specific substituted diamines and of hexamethylenediamine were used as initial compounds in the polycondensation. These amides contained equimolecular quantities of diamine and dibasic acid; all crystallized nicely except the amide of N-monoisopropylhexamethylenediamine which separated out of solution as an oil. The polycondensation was conducted under the conditions usually used to obtain polyamides in the absence of a solvent [6].

In order to investigate the effect of degree of substitution on the properties of a polyamide, we polycondensed the following mixture: 1) 75% of hexamethylenediamine adipamide + 25% N,N'-diisopropylhexamethylenediamine adipamide. As compared to pure AH* polycondensation product, this polymer should theoretically contain 25% N-substituted groups. 2) We used 50 mole % hexamethylenediamine adipamide + 50 mole % N,N'-diisopropylhexamethylenediamine adipamide. 3) We used 25 mole % hexamethylenediamine adipamide + 75 mole % N,N'-diisopropylhexamethylenediamine adipamide. Depending on the degree of substitution, the polyamides are conventionally designated as: "N-isopropyl-substituted 75 : 25, 50 : 50, 25 : 75" respectively.

A polyamide was prepared through polycondensation of N-monoisopropylhexamethylenediamine with adipic acid (in equimolar ratio) so as to compare the effectiveness of substitution with respect to the relative amounts of N,N'-di- or N-monoalkylated diamines in the polymer structure (at an equal over-all degree of N-substitution, 50%); its properties are compared with those of a "N-isopropyl-substituted 50 : 50" polyamide obtained through polycondensation of a N,N'-disubstituted and unsubstituted diamine mixture with adipic acid.

We have established that as the number of N-substituted groups increases, a greater solubility in a series of organic solvents becomes apparent. The melting point of polymers is lowered too (Fig. 1). A comparison of properties among polyamides obtained by using N,N'-di- and N-monosubstituted diamines at an equal over-all degree of substitution shows that the use of N-monosubstituted diamine results in the formation of a product which is characterized by a lowered melting point, an increased solubility in organic solvents (in comparison to a product based on N,N'-disubstituted diamine), and a lack of brittleness at ordinary temperatures (Table 1).

TABLE 1

The Effect of Substitution Sequence on the Properties of Polyamides

| N-isopropyl substituted polyamide (50% substitution) | Melting point | Solubility | |
|---|---|---|---|
| | | ethyl alcohol | acetone |
| Based on N,N'-disubstituted diamine | 185° | – | – |
| Based on N-monosubstituted diamine | 74 | + | + |

The differences shown in the properties of polyamides could be explained by variations in the degree of regularity in the chain structure, depending on whether N-mono- or N,N'-dialkylated diamines were used.

## EXPERIMENTAL

The polycondensation process was carried out in an apparatus shown in Fig. 2. The pyrex apparatus was assembled from sections and consisted of: a reaction flask, an adapter supplied with an electric heater, and a thermally insulated column packed with glass coils. An extension tap to connect the apparatus to a vacuum system through an outlet could replace the column. A capillary was lowered into the reaction flask for the purpose of bubbling nitrogen, since the polycondensation was conducted under a nitrogen atmosphere. Such an apparatus had been used [7] for the synthesis of polyesters. The nitrogen was carefully purified from hydrogen and dried with concentrated sulfuric acid and phosphorus pentoxide. The apparatus was heated in a ditolylmethane bath. Hexamethylenediamine, N,N'-diisopropylhexamethylenediamine, and N-monoisopropylhexamethylenediamine adipamides were the starting materials in the polycondensation. The preparation of amides was reduced to the following operations. Adipic acid was dissolved in ethyl alcohol with heating. Next, a 5% excess of diamine (over 1 : 1 acid-diamine ratio) was added to the solution, the mixture was heated to the boiling point of water bath, and after completion cooled in ice. At this stage crystalline amide precipitated. This amide was washed with ethyl alcohol on a suction funnel and dried at 100°. The amide of N-mono-substituted diamine did not crystallize, but settled out as an oil.

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* AH is an accepted abbreviation for hexamethylenediamine adipamide.

To 58.4 g of adipic acid in 100 ml of ethyl alcohol we added 48.7 g of hexamethylenediamine. We obtained 96.2 g of amide (92% yield from the acid used in reaction). M.p. 190°.

To 58.4 g of adipic acid in 135 ml of ethyl alcohol we added 84.0 g of N,N'-diisopropylhexamethylenediamine. We obtained 131.4 g (95%) of amide. M.p. 168°.

To 58.4 g of adipic acid in 120 ml of ethyl alcohol we added 66.3 g of N-monoisopropylhexamethylenediamine. We obtained 105.8 g of amide (in the form of an oil), yield 87%.

In all the cases (computed from molecular weights) the molar diamine—acid ratio was 1 : 1 in the salts prepared.

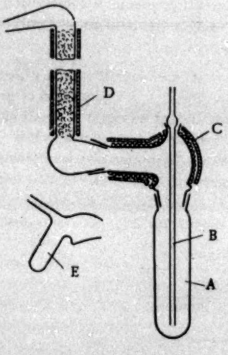

Fig. 2. Apparatus for conducting polycondensation reactions.
A) Reaction vessel; B) capillary; C) adapter; D) column; E) an extension tap for connecting to a vacuum system.

The polycondensation experiments were conducted in the following manner. A mixture of amides was placed in the reaction flask. The apparatus was lowered into a bath, the heat was turned on, and nitrogen was bubbled through. Since the amides were nonvolatile we had no use for the packed column and right away hooked to the apparatus the extension tap into which went the water formed in the reaction. The bath temperature was raised to 220° and the mixture kept at this temperature until no more water was being driven off. The adapter was heated with a coil to prevent water from condensing and returning into the reaction flask. The apparatus was then connected to a vacuum system, suction was applied, and gradually the residual pressure was reduced to 0.8-0.4 mm. The bath temperature was gradually increased so as to keep all the polymers liquid and allow nitrogen bubbles to pass through the reaction mixture. The reaction was judged to be complete when the weight of reaction mixture ceased diminishing (the apparatus with capillary and adapter was weighed under nitrogen) after cooling. After completion of reaction, the polymers were poured out into porcelain evaporating dishes and cooled in a desiccator. Table 2 lists the ratios of components used in the polycondensation for the purpose of getting polyamides possessing various degrees of alkylation. The reaction was conducted for 20 hours at atmospheric pressure and 220°, and for 10 hours at the final 0.4 mm pressure and 250°. Table 3 shows other characteristic properties of polyamides obtained by us.

All the investigated N-alkylated polyamides are soluble in formic acid, insoluble in water, ether, petroleum ether, and benzene. Only N-isopropyl-substituted 25 : 75 and N-isopropyl-substituted 50 : 50 (with regular structure) are soluble in ethyl alcohol.

TABLE 2

Experimental Data From the Preparation of N-Alkylated Polyamides

| Amide AH (g) | Adipamide of N-substituted hexamethylenediamine | Weight (in g) | Ratio AH : amide of substituted diamine | Designation of polyamide |
|---|---|---|---|---|
| 21.00 | N,N'-Diisopropylhexamethylenediamine | 9.25 | 75 : 25 | N-Isopropyl-substituted 75 : 25 |
| 12.00 | The same | 15.90 | 50 : 50 | The same 50 : 50 |
| 6.00 | The same | 23.68 | 25 : 75 | The same 25 : 75 |
| – | N-Monoisopropylhexamethylenediamine | 28.00 | 0 : 100 | The same 50 : 50 with regular structure |

TABLE 3

Some Properties of N-Alkylated Polyamides

| Polyamides | Melting point (following Kramer-Sarnov) | Viscosity (η) | | Remarks |
|---|---|---|---|---|
| | | specific of 3.0% alcoholic solution | absolute | |
| N-Isopropyl-substituted 75 : 25 | 248° | – | – | Hard, brittle |
| N-Isopropyl-substituted 50 : 50 | 185 | – | – | Same |
| N-Isopropyl-substituted 25 : 75 | 54 | 0.561 | 0.170 | Soft, possesses some elasticity |
| N-Isopropyl-substituted 50 : 50 with regular structure | 74 | 0.682 | 0.166 | Same |

## SUMMARY

1) By starting with N,N'-di- and N-monoisopropylhexamethylenediamine and adipic acid we obtained and characterized polyamides with a varying degree and sequence of N-substitution.

2) We have established that an increase in degree of substitution improves the solubility of polyamides, gradually lowers the melting point, and decreases the brittleness of polymers. Regular substitution is more effective as compared to irregular of the same degree.

## LITERATURE CITED

[1] O. Fuchs, Kunststoffe, 443, 40 (1953).

[2] P. P. Kobeko, Amorphous Substances, Izd. AN SSSR (1952).*

[3] E. I. Barg, Technology of Synthetic Plastics, State Sci.-Tech. Chem. Lit. Press, 117 (1954).*

[4] B. S. Biggs, C. J. Frosch and R. H. Erickson, Ind. Eng. Ch. 38, 1016 (1946).

[5] E. L. Wittbecker, R. C. Houts and W. W. Watkins, Ind. Eng. Ch. 40, 875 (1948).

[6] V. V. Korshak, S. R. Rafikov, Synthesis and Study of High Molecular Compounds, Izd. AN SSSR, 240 (1949).*

[7] B. S. Biggs, R. H. Erickson and C. S. Fuller, Ind. Eng. Ch. 39, 1090 (1947).

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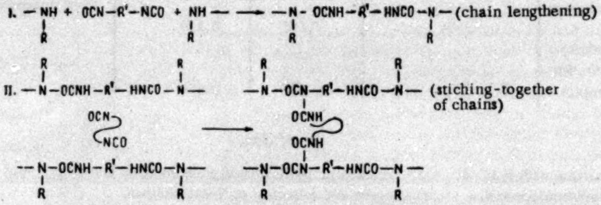
*In Russian.

# A STUDY IN THE FIELD OF SYNTHESIS OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE AND THEIR POLYCONDENSATION

## VII. PREPARATION OF COMPLETELY N-ALKYLATED POLYAMIDES AND COUPLING OF THEIR CHAINS WITH A DIISOCYANATE

A. L. Klebanskii and M. S. Vilesova

The use of diisocyanates for lengthening or "stitching-together" of chains of polyesters has been described extensively [1]. This method is used here for the first application to N-substituted polyamides and is used in two stages: 1) the preparation of completely N-substituted polyamides from adipic acid and N,N'-dialkylhexamethylenediamine with various substituents as the radicals, and 2) the lengthening of the chains of the resulting polyamide and the transformation of the linear polymer into a tridimensional polymer by the reaction with a diisocyanate according to the reaction scheme:



Thus, the first stage consists of the preparation of a polyamide based on a N,N'-dialkylated diamine which leads to the formation of a completely N-substituted polymer which is characterized by the lowered intermolecular interaction as a result of the introduction of the substituents at the nitrogen, which totally destroy the hydrogen bonds and reduce the van der Waals forces.

In order to insure the formation of the link of the polyamide chains (during their lengthening) by the diisocyanate predominantly with the typical carbamido links, it was necessary to prepare a polymer with secondary amino groups at the chain ends. In a case in which the ends of the polyamide chains are terminated by carboxyl groups the link with the diisocyanate would be formed in the shape of an amide linkage and would be accompanied by evolution of carbon dioxide which is naturally undesirable owing to the formation of pores in the polymer mass. For preparation of a polyamide with terminal secondary amine groups there was taken an excess of the diamine for the polycondensation reaction. In connection with this, the starting reaction components were not the salts but the free substituted diamine and adipic acid. The reaction of polycondensation was run during the initial period in an apparatus provided with a packed column for prevention of volatilization of the diamine [2] at 150-200°. The formula suggested by V. V. Korshak et al.[3] was used for the preliminary calculation of the necessary amount of excess substituted diamine.

The experiments with the preparation of N-substituted polyamides were run with a 10 mole percent excess of the diamine.

In order to prepare the starting polymers, in the synthesis of N-substituted polyamides, for the subsequent treatment with diisocyanate the following diamines were used for the polycondensation reaction with adipic acid: N,N'-di-n-propyl, N,N'-diisopropyl, N,N'-di-n-butyl and N,N'-di-2-butyl-hexamethylenediamines. Some of the properties of the polymers prepared by us are shown in Tables 1 and 2.

TABLE 1

Solubility of N-Alkylated Polyamides Prepared

| Polyamide | Solubility | | | | | |
|---|---|---|---|---|---|---|
| | $H_2O$ | alcohol | ether | benzene | chloro-benzene | pyridine |
| N-n-propyl substituted | — | + | — | + | + | + |
| N-Isopropyl substituted | — | + | — | — | + | + |
| N-n-Butyl substituted | — | + | — | + | + | + |
| N-2-Butyl substituted | — | + | — | — | + | + |

TABLE 2

Some Properties of the N-Alkylated Polyamides Prepared

| Polyamide* | Content of active H per 100 g of the polymer (in mg) | Molecular wt. by end groups** | Viscosity ($\eta$) | |
|---|---|---|---|---|
| | | | specific, of 3% alcoholic solution | character-istics |
| N-n-Propyl-substituted | 66.5 | 3000 | 0.265 | 0.066 |
| N-Isopropyl-substituted | 82.9 | 2400 | 0.260 | 0.060 |
| N-n-Butyl-substituted | 55.2 | 3600 | 0.398 | 0.088 |
| N-2-Butyl-substituted | 72.0 | 2800 | 0.300 | 0.050 |

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* By Chugaev-Tserevitinov method.

** The alcoholic solution was always basic.

The data in Table 2 make it evident that no significant differences in the magnitudes of molecular weights or characteristic viscosity can be observed among the polyamides with various substituents. The effect of the structure of the substituting radical is manifested in the solubility of the polymers and in the consistency (at normal temperature): polyamides having the normal substituent radical are balsam-like and are readily soluble in benzene, while those with a branched substituent radical are waxy and are insoluble in benzene. The determination of the number of end groups in completely N-alkylated polyamides plays a very significant role since on the basis of the thus obtained values one calculates the amount of the diisocyanate necessary for the lengthening and spatial cross-linking of the polyamide chains.

The determination of the number of end groups was done on the basis of polymer analysis for the content of active hydrogen by the method of Chugaev-Tserevitinov. This method permits one to determine both the secondary amino groups and the carboxyl groups which may exist in small amounts at the chain ends despite the excess amount of the diamine used in the polycondensation reaction.

For running the analysis we used chlorobenzene in the present work, this substance having turned out to be a good solvent for the Chugaev-Tserevitinov reaction. Chlorobenzene dissolves the N-substituted polyamides prepared by us, does not yield gaseous products after the addition of methylmagnesium iodide and has a relatively

TABLE 3

Change of Viscosity of 100%-Substituted Polyamides After Treatment with Diisocyanate

| Substituent radical | Specific viscosity of 3% alcoholic solution | |
|---|---|---|
| | Starting polymer | Polymer after treatment with diisocyanate |
| n-Propyl substituted | 0.265 | 0.641 |
| Isopropyl substituted | 0.260 | 0.806 |
| n-Butyl substituted | 0.398 | 1.249 |
| 2-Butyl substituted | 0.300 | 0.972 |

low magnitude of the vapor pressure at the temperature of the determination (6.6 mm at 15°). On the basis of the determination of the number of end groups one may calculate the average numerical molecular weight of the polyamide.

The second stage of the reaction, being considered here, consists, as indicated earlier, of the reaction of the completely N-alkylated polyamides with diisocyanate. 2,4-Toluylenediisocyanate, which had been recommended for similar reactions with polyesters as one of the reactive diisocyanates, was used by us as the agent for chain lengthening of the starting polyamide and for the cross-linking. Initially the chain lengthening of the starting polyamide was run by the addition to the polymer of 2,4-toluylenediisocyanate in an amount calculated at 95 mole % of isocyanate groups per 100 mole % of end groups of the polyamide, followed by heating of the mixture at 130°. The reaction of the isocyanate groups with the NH- or the COOH groups proceeds very rapidly under these conditions, which fact agrees with the literature data on the polyesters. In the present case the reaction rate was controlled by the alteration of viscosity of the polymer solutions. The viscosity of the polymers rose considerably after the addition of the diisocyanate and elevation of the temperature of the reaction mixture to 130°, but the viscosity was almost unaltered on further heating.

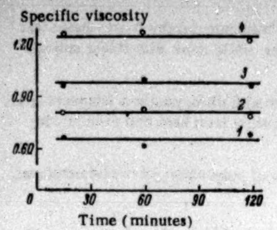
The viscosity of the solutions of N-substituted polyamides after the reaction with diisocyanate rises approximately 2.5-3-fold (see Table 3) which fact indicates the chain lengthening and the corresponding increase of the molecular weight of the polymers. However the polymers retain the ability to dissolve in alcohol and the ability to melt which indicates the absence of tridimensional links in them.

Polyamides with branched substituents at the nitrogen (isopropyl, 2-butyl) form hard brittle polymers as the result of reaction with 2,4-toluylenediisocyanate. Polyamides with normal substituent radicals (n-propyl, n-butyl) form elastic polymers. The observed influence of the radical structure (normal and branched) on the physico-mechanical properties of the polyamides agrees with the known data relative to the polyacrylates which are substituted in the chain.

The reaction of spatial interbinding of polyamide chains of the above-indicated structure was realized on an example of the N-isopropyl and N-n-butyl substituted polyamides (after lengthening of their chains by the diisocyanate). The stitching-together (or cross-linking) of the chains was done by prolonged heating (10-12 hours at 150°) of the polymer with additionally added amount of the diisocyanate which reacts with the active hydrogen of the carbamido groups formed in the process of chain lengthening. After the indicated time interval, the polyamides lose the ability to melt and to dissolve (in alcohol), which facts permit us to conclude that a tridimensional structure had formed.

## EXPERIMENTAL

The experiments on the preparation of totally N-alkylated polyamides were run in equipment which had been described earlier [2]. Owing to the fact that the polymer formed by this method arises with an excess of the diamine, which locates itself at the chain ends, the preliminary preparation of salts was needless. The reaction mixture was a mixture of adipic acid and the corresponding diamine. For prevention of the loss of the diamine in the nitrogen stream at elevated temperature, the apparatus was provided with a column with a packing for the first stage of the reaction (heating at atmospheric pressure) and the elevation of temperature of the heating bath was done gradually. Heating of the distillate for complete distillation of the resulting water was also switched



Dependence of specific viscosity on the duration of heating of polyamide with diisocyanate.
1) N-n-Propyl substituted; 2) N-isopropyl substituted; 3) N-n-butyl substituted; 4) N-2-butyl substituted.

on after the passage of a certain period of time after the beginning of the reaction. For running the reaction in vacuum the column was replaced by a takeoff tube. The maximum reaction temperature reached 220°. In other respects the reaction was run under the same conditions as in the case of preparation of partially N-alkylated polyamides. The following amounts of components were used for running the polycondensation:

1) 12.1 g of adipic acid and 18.3 g of N,N'-di-n-propylhexamethylenediamine; the resulting polyamide was designated as N-n-propyl substituted.

2) 16.6 g of adipic acid and 25.0 g of N,N'-diisopropylhexamethylenediamine; polyamide notation – N-isopropyl substituted.

3) 14.5 g of adipic acid and 25.0 g of N,N'-di-n-butylhexamethylenediamine; polymer designation – N-n-butyl substituted.

4) 14.5 g of adipic acid and 25.0 g of N,N'-di-2-butylhexamethylenediamine; polymer designation – N-2-butyl substituted.

The excess of the diamine in the starting mixture was 10 mole % in all cases. The reaction time was 20 hours at atmospheric pressure and temperature of 150°, 20 hours at atmospheric pressure and 200°, 10 hours at the pressure of 0.4 mm and 220°. During the reaction the following number of grams of water was distilled in the experiments: 1) 2.9, 2) 3.9, 3) 3.5, and 4) 3.4. The excess diamine which failed to react was also distilled off.

The content of active end groups by the Chugaev-Tserevitinov method was done (the sum of COOH and NHR groups) for the reaction of the completely N-alkylated polyamides with 2,4-toluylenediisocyanate and for the calculation of the necessary amount of the latter for the purpose of chain lengthening in the polymer; the data are given in Table 2.

The reaction of chain lengthening by the diisocyanate was run in a flask with about 70 ml capacity, provided with a stirrer and a reflux condenser, placed in an oil bath. The N-substituted polyamide was placed into the flask and to it there was added the calculated amount of the diisocyanate (95% of isocyanate groups per 100% of polyamide end groups) and the mixture was heated with stirring at 130°. The reaction mixture was maintained at this temperature and after definite time intervals samples were taken from it for the determination of change in viscosity of the polymer (see figure). During the reaction the evolution of gaseous products was observed ($CO_2$).

For 25.0 g of N-n-propyl substituted polyamide there was taken 1.38 g of 2,4-toluylenediisocyanate; for 30.0 g of N-isopropyl substituted polyamide – 2.06 g of the diisocyanate; for 30 g of N-n-butyl substituted polyamide – 1.37 g of diisocyanate; and for 30.2 g of N-2-butyl substituted polyamide – 1.79 g of diisocyanate.

The reaction of tridimensional linking of the lengthened N-alkylated polyamide chains by means of the diisocyanate at the carbamido groups, which had formed during the chain lengthening of the original polyamide, was run in an air thermostat at 150-155°. The polyamide that had been "lengthened" by the diisocyanate was melted in a porcelain dish, an additional amount of diisocyanate (Table 4) was added to it, the mixture was stirred thoroughly and maintained in the thermostat for a long interval of time. We succeeded in forming a tridimensional structure only after the addition of a considerable excess of the diisocyanate – of the order of 12 weight %. The loss of solubility and the ability to melt in the polymer indicated the formation of the tridimensional structure. The corresponding data are shown in Table 4.

TABLE 4

Data of Experiments on Formation of Cross-Linked Polyamides

| Initial polyamide | Amount (in g) | 2,4-Toluylene-diisocyanate (g) | Solubility of polymer in alcohol after heating at 150° for period shown (hours) | | | | |
|---|---|---|---|---|---|---|---|
| | | | 1 | 3 | 6 | 9 | 12 |
| N-Isopropyl substituted | 20.00 | 2.20 | + | + | + | – | – |
| N-n-Butyl substituted | 20.00 | 2.40 | + | + | + | + | – |

## SUMMARY

1. Completely N-alkylated polyamides were prepared with various substituents; hereby it was shown that polyamides with branched radicals (isopropyl, 2-butyl) have a waxy character, while those with linear radicals (n-propyl, n-butyl) are balsam-like and soluble in benzene.

2. It was established that in the interaction of N-alkylated polyamides with diisocyanate a lengthening of the chains of the former takes place; here the polymers with branched substituents form hard and even brittle products, while those with linear substituents form elastic products.

3. A second treatment with excess diisocyanate leads to the formation of polyamides with tridimensional structure.

## LITERATURE CITED

[1] O. Bayer, E. Müller, S. Petersen, H. F. Piepenbrink and E. Windemuth, Angew. Chem. 62, 57 (1950); E. Müller, O. Bayer, E. Petersen, H. F. Piepenbrink, G. Schmidt and E. Weinbrenner, Angew. Chem. 64, 323 (1952).

[2] A. L. Klebanskii and M. S. Vilesova, J. Gen. Chem. 28, 1066 (1958).*

[3] V. V. Korshak and V. V. Golubev, Bull. Acad. Sci. USSR, Div. Chem. Sci. 185, 1946.

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*Original Russian pagination. See C. B. Translation.

# SYNTHESIS OF 2-ETHYL- AND 2-PROPYL-1,3-BUTADIENES

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and M. F. Egudina

The literature on the synthesis of β-substituted diene hydrocarbons is a rather limited [1, 2]. The most acceptable amount of described methods of synthesis are those based on pyrolysis of the corresponding acetates [3-5]. The method of preparation of β-alkylbutadienes, proposed by Carothers [6], from α-chloromethylallene and alkylmagnesium halides was not used owing to the difficulty of preparation of the α-chloromethylallene.

It was shown in our laboratory that during the continuous running of the process of hydrochlorination of vinylacetylene in the presence of cuprous chloride under certain conditions it is possible to obtain up to 50% of α-chloromethylallene, along with chloroprene [7]. This fact led us to undertake anew a study of synthesis of butadienes from α-chloromethylallene. We prepared 2-ethyl- and 2-propyl-1,3-butadienes by the action of corresponding alkylmagnesium halides on this substance. The yield of alkylbutadienes did not rise above 26% under the conditions explored by us, this being caused by a number of side reactions.

From the by-products of the reaction there were isolated: the dimer of propyl-1,3-butadiene, n-hexane and 1,3-hexadiene. The formation of the latter may be explained by replacement of chlorine by an alkyl group in α-chloromethylallene with the subsequent isomerization of the resulting allenic compound into the diene.

In addition, in all cases there was obtained a considerable amount of polymers which was evidently connected with the possibility of a condensation of two molecules of α-chloromethylallene with formation of octatetraene (with allenic structure) and subsequent isomerization of it into a compound with a conjugated double bond system, which compound polymerized under the experimental conditions used.

$$CH_2=C=CH-CH_2-CH_2-CH=C=CH_2 \rightarrow CH_2=CH-CH=CH-CH=CH-CH=CH_2$$

The properties of the alkylbutadienes prepared by us are given in the table. The unsaturation of the hydrocarbons was determined by the titration with bromine according to Kaufman, by bromide-bromate and bromoiodine methods. The best results were obtained with the Kaufman solution, but even in this case the addition of bromine proceeded very slowly, so that for complete reaction the sample must stand for 2-3 days. Thus, for example, the unsaturation of ethylbutadiene as determined by standing for one day was 80%, after two days it was 94%, after three days it was 97% and after seven days it was 97%.

For proof of the diene structure the alkylbutadienes were condensed with maleic anhydride in benzene solution. The reaction proceeded very violently and began immediately on mixing the benzene solutions of alkylbutadiene and maleic anhydride. The melting points of the products thus prepared are shown in the table.

## EXPERIMENTAL

The preparation of α-chloromethylallene was described by us earlier [7, 8].

The synthesis of 2-ethylbutadiene was carried out in the following fashion. To an ethereal solution of the organomagnesium compound, prepared from magnesium shavings and ethyl chloride in a three-liter flask with four necks, there was added, with energetic stirring, the α-chloromethylallene at such a rate that the reaction temperature failed to rise over 40°. The organomagnesium compound was taken in 10% excess relative to the α-chloromethylallene. After the addition of the entire amount of α-chloromethylallene, the agitation of the thick reaction

Properties of Alkylbutadienes

| Substance | Boiling point | $d_4^{20}$ | $n_D^{20}$ | Molecular weight (cryoscopic) |  | $MR_D$ |  | M.p. of adduct with maleic anhydride |  | Carbon (in %) |  | Hydrogen (in %) |  | Remarks |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  | found | calc. | found | calc. | before hydrolysis | after hydrolysis | found | calc. | found | calc. |  |
| 2-Ethyl-1,3-butadiene | 65—66° | 0.7197 | 1.4328 | 81.60 | 82.14 | 29.62 | 28.97 | 67—68° | 140° | 87.94 | 87.73 | 12.10 | 12.27 | Our data |
|  | 66 | — | 1.4325 | — | 82.14 | — | 28.97 | 67—69 | — | — | — | — | — | [4] |
|  | 66.6 | 0.7154 | 1.4328 | — | 82.14 | 29.76 | 28.97 | — | — | — | — | — | — | [9] |
| 2-Propyl-1,3-butadiene* | 92—93 | 0.7313 | 1.4361 | 96.30 | 96.16 | 34.33 | 33.59 | 47—48.5 | 161 | 87.08 | 87.43 | 12.70 | 12.57 | Our data |

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* 2-Propyl-1,3-butadiene had not been described in the literature.

mixture was continued for 2-3 hours, after which the decomposition of the excess organomagnesium compound and the formed complex was done by means of a cooled saturated solution of ammonium chloride and 5% hydrochloric acid. The ethereal layer was separated, washed with cooled saturated solution of ammonium chloride and dried over calcined magnesium sulfate. After the removal of ether, the reaction products were distilled in vacuum and then were distilled twice through an effective column with a Nichrome packing.

The working-up of the reaction products was done as follows in one of the first experiments. After completion of the reaction and the layering-out of the ether, the latter was separated from the crystalline residue. The residue was washed with absolute ether and the ethereal solutions were combined (first ethereal extract). Then the crystalline residue was treated with a cooled saturated solution of ammonium chloride. Heat evolution was observed and part of the crystalline residue dissolved. The oily layer which formed thereby was separated. Organic substances were extracted with ether from the aqueous layer along with the crystalline residue and the ethereal extract was added to the oily layer (second ethereal extract). Then, the aqueous solution with the precipitate was treated with 5-10% hydrochloric acid until the precipitate dissolved. The organic matter was extracted from the acidic aqueous solution with ether (third ethereal extract). All the ethereal extracts were dried with calcined magnesium sulfate, after which each extract was worked up separately; the ether was distilled off and the organic residue was subjected to fractionation. As the result of such treatment it was shown that no organic residue was contained in the third ethereal extract, while the first and the second extracts contained approximately equal (by weight) amounts of organic products, the composition of which was almost the same. Thus one may conclude that in the process of the reaction there is formed a complex which decomposes partially even prior to the addition of the aqueous solution of ammonium chloride. Starting with this conclusion, the above separate working-up of the condensation products was not used in the subsequent experiments.

Two fractions were isolated from the by-products in the synthesis of ethylbutadiene:

1st: b.p. 73-75°, $d^{20}_4$ 0.7495, $n^{20}D$ 1.4190, M 81.12;
2nd: b.p. 43-45° (20 mm), $d^{20}_4$ 0.8308, $n^{20}D$ 1.4370, M 125.7.

Found %: C 76.46, 76.30; H 10.85, 11.03; Cl 5.46.

The first fraction was obtained in negligible amounts when the reaction was run in diethyl ether and was the principal fraction when the reaction was run in dibutyl ether.

It was established that this fraction contains about 50% of 1,3-hexadiene (by test reaction with maleic anhydride), a certain amount of carbonyl compounds the structures of which were not determined, and about 5% of α-chloromethylallene (by content of hydrolyzable chlorine).

The certain discrepancy of the constants of the first fraction with the literature data on 1,3-hexadiene is evidently explained by the presence of admixed carbonyl compounds of α-chloromethylallene.

The second fraction contains about 50% of dienic compound and in it, according to infrared spectroscopic data, there is a certain amount of allenic compounds (infrared spectrum shows the 5.09 μ band). One may suppose that the hydrocarbon contained in the second fraction is the above-mentioned octatetraene with admixture of other compounds whose composition was not determined. The formation of butane (from ethyl bromide by the Wurtz reaction) was not observed at all.

From the by-products in the synthesis of propylbutadiene, which was carried out under the same conditions as the synthesis of ethylbutadiene, there were isolated: (b.p. 68°, $d^{20}_4$ 0.656, $n^{20}D$ 1.3760) and the dimer of propylbutadiene.

B.p. 93° (4 mm), $d^{20}_4$ 0.8537, $n^{20}D$ 1.4751, $MR_D$ 63.38; calculated 63.72.
Found: M 191.65. $C_{14}H_{24}$. Calculated: M 192.33.

## SUMMARY

1. 2-Ethyl and 2-propyl-1,3-butadienes were synthesized by the action of corresponding organomagnesium compounds on α-chloromethylallene. The latter product is being described for the first time.

2. A dimer of 2-propyl-1,3-butadiene was isolated from the by-products of the synthesis of propylbutadiene and suitably characterized.

## LITERATURE CITED

[1] Pariselle and Simon, Compt. rend. 173, 86 (1921).

[2] Braun and Keller, Ber. 64, 2617 (1931).

[3] C. S. Marvel, J. Am. Chem. Soc. 70, 1694 (1948).

[4] C. S. Marvel, J. Am. Chem. Soc. 70, 3842 (1948).

[5] C. G. Overberger, J. Am. Chem. Soc. 73, 2540 (1951).

[6] W. H. Carothers and G. J. Berchet, J. Am. Chem. Soc. 55, 2813 (1933).

[7] I. M. Dolgopol'skii and Iu. V. Trenke, Report of All-Union Research Institute for Synthetic Rubber, No. 1947 (1949).*

[8] I. M. Dolgopol'skii, I. M. Dobromil'skaia, A. V. Tumanova and M. F. Egudina, Report of All-Union Research Institute for Synthetic Rubber, No. 759 (1957).*

[9] I. A. Livshits and L. M. Korobova, Report of All-Union Research Institute for Synthetic Rubber, No. 3911 (1954).*

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*In Russian.

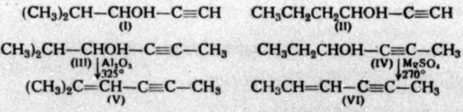
# HOMOLOGS OF MONOVINYLACETYLENE

## VII. DEHYDRATION OF SECONDARY ACETYLENIC ALCOHOLS

I. A. Favorskaia, E. M. Auvinen and Iu. P. Artsybashev

Hydrocarbons of the vinylacetylene series with alkyl substituents at the terminal carbon atoms of the conjugated system may be prepared by dehydration of secondary acetylenic alcohols. Such vinylacetylenic hydrocarbons have been of interest to us from the point of view of a study of their styrene-type dimerization [1].

The dehydration of four secondary acetylenic alcohols: isopropylethynylcarbinol (I), n-propylethynylcarbinol (II), isopropyl (methylethynyl)-carbinol (III) and ethyl(methylethynyl)carbinol (IV), was studied in the present investigation.



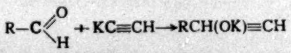
$(CH_3)_2CH{-}CHOH{-}C{\equiv}CH$ (I)  $CH_3CH_2CH_2CHOH{-}C{\equiv}CH$ (II)

$(CH_3)_2CH{-}CHOH{-}C{\equiv}C{-}CH_3$ (III) $\xrightarrow[325^\circ]{Al_2O_3}$ $(CH_3)_2C{=}CH{-}C{\equiv}C{-}CH_3$ (V)

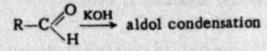
$CH_3CH_2CHOH{-}C{\equiv}C{-}CH_3$ (IV) $\xrightarrow[270^\circ]{MgSO_4}$ $CH_3CH{=}CH{-}C{\equiv}C{-}CH_3$ (VI)

Alcohols (I) and (II) were prepared by us according to A. E. Favorskii's method in yields of 60-65%. The condensation of aldehydes with acetylene according to the A. E. Favorskii's method may be realized in good yields under the conditions of slow addition of greatly diluted ethereal solution of the aldehyde to the reaction mixture.

The aldehyde may react in two directions under the conditions of the Favorskii reaction:



$$R{-}C\begin{smallmatrix}\nearrow O\\ \searrow H\end{smallmatrix} + KC{\equiv}CH \rightarrow RCH(OK){\equiv}CH \quad (1)$$



$$R{-}C\begin{smallmatrix}\nearrow O\\ \searrow H\end{smallmatrix} \xrightarrow{KOH} \text{aldol condensation} \quad (2)$$

If the rate of the first condensation reaction is sufficiently great, then owing to the absence of excess aldehyde in the reaction mixture, the aldol condensation does not take place.

We set up a large number of experiments on dehydration of secondary acetylenic alcohols—isopropylethynylcarbinol (I) and n-propylethynylcarbinol (II). In catalytic dehydration over $Al_2O_3$, $NH_4H_2PO_4$ on carbon and pumice, unfired porcelain and $MgSO_4$ at 250-300° the alcohols (I) and (II) were mainly recovered unchanged. Raising the temperature of dehydration to 320° also failed to lead to even traces of hydrocarbons. Therefore it was evident that secondary $\alpha,\beta$-acetylenic alcohols with a terminal acetylenic group, (I) and (II) do not lose water under conditions which are usual for catalytic dehydration of tertiary $\alpha,\beta$-acetylenic alcohols.

We also attempted to realize the transition from alcohol (I) to the hydrocarbon, 2-methyl-2-penten-4-yne, through the ester of p-toluene-sulfonic acid [2], but the reaction of decomposition of the sulfonate led to formation of resinification products or, in the case of decomposition by means of sodium alcoholate, to the formation of a mixture of substances containing an ethoxyl group. The starting materials for the synthesis of hydrocarbons with substituents at both ends of the conjugated system – 2-methyl-2-hexen-4-yne (V) and 2-hexen-4-yne (VI), were the corresponding secondary acetylenic alcohols – isopropyl (methylethynyl)-carbinol (III) and ethyl(methylethynyl)carbinol (IV). In running the synthesis of these alcohols by the Iotsich method it was established that the yield of the alcohols is raised if the reaction mixture, after the addition of the aldehyde, is heated on a water bath for 4-5 hours and is left to stand for 5-6 days.

Vinylacetylenic hydrocarbons: 2-methyl-2-hexen-4-yne (V) and 2-hexen-4-yne (VI) were prepared by dehydration of these alcohols (III) and (IV). These hydrocarbons fit, respectively, the formulas $C_7H_{10}$ and $C_6H_8$ in their elemental composition and molecular weight. The hydrocarbons added to the theoretical amount of hydrogen, calculated for one double and one triple bond, during catalytic hydrogenation over platinum black.

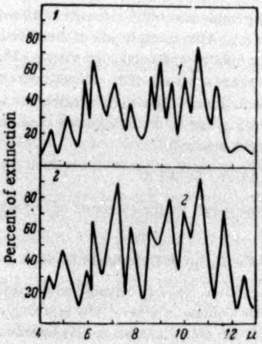
Physical Properties of Hydrocarbons (V) and (VI)

| Hydro-carbon | $d_4^{20}$ | $n_4^{20}$ | $n_F^{20}$ | $n_C^{20}$ | $MR_D$ |  | $ME_D$ | $\omega_{F,C,D}$ |
|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  | found | calc. |  |  |
| (V) | 0.7849 | 1.46595 | 1.47684 | 1.46232 | 33.21 | 32.06 | 1.15 | 31.16 |
| (VI) | 0.7703 | 1.46339 | 1.47431 | 1.45926 | 28.67 | 27.44 | 1.23 | 32.47 |

Exaltation of molar refraction is equal to one unit on the average [3, 4] in the series of vinylacetylenic hydrocarbons of type:

$$R-CH=CH-C\equiv C-R$$

The magnitude of relative dispersion also permits us to draw the conclusion about the presence in hydrocarbons (V) and (VI) of a system of conjugated bonds [5]. The structure of hydrocarbon $C_7H_{10}$ (V) was proved by the way of oxidation and ozonolysis.



Infrared absorption spectra of 2-hexen-4-yne (1) and 2-methyl-2-hexen-4-yne (2).

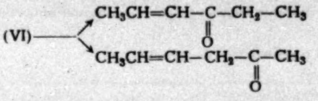
As the result of the oxidation there were isolated acetone, acetic and oxalic acids. The absence of the possible isomerization product with a terminal methylene group was established by ozonolysis of hydrocarbon (V) [9]. These data permitted us to assign the structure of 2-methyl-2-hexen-4-yne to hydrocarbon (V). The chemical proof of structure was confirmed spectroscopically by taking the spectrum in the infrared region (see figure). On the basis of refractometric data and the infrared spectrum (see figure) the structure of a conjugated vinylacetylenic hydrocarbon – 2-hexen-4-yne, was assigned to hydrocarbon $C_6H_8$ (VI).

It is evident in the examination of the infrared spectra of the hydrocarbons under study that both hydrocarbons are substituted vinylacetylenic hydrocarbons: the absorption bands which correspond to the bond vibrations of the double and the doubly substituted triple bonds are somewhat shifted from their normal positions owing to the conjugation (V) 1613 $cm^{-1}$, 2270 $cm^{-1}$, and (VI) 1607 $cm^{-1}$, 2270 $cm^{-1}$ [6, 7]. The structure of hydrocarbon (V) as that of an enyne hydrocarbon containing a triply substituted double bond is confirmed by the following data: the deformational nonplanar vibrations of the C–H bond in the system $RCH=CRR_2$ (trisubstituted ethylene) are characterized by absorption in the region of 800-840 $cm^{-1}$ [8]. A frequency of 856 $cm^{-1}$ was found in the spectrum [9] of the enyne hydrocarbon – 3,5-dimethyl-3-hexen-1-yne, at the infrared region. A frequency of 859 $cm^{-1}$ was discovered in the spectrum of hydrocarbon (V). Hydrocarbon (V) does not contain any admixture of the isomer with a terminal methylene group, since the frequencies 903 and

1410 cm$^{-1}$ are absent from its spectrum [6, 9]. This conclusion coincides completely with the ozonolysis data.

The infrared spectrum of hydrocarbon (VI) is not discussed in detail in this paper since the separation of it into cis and trans isomers was not performed by us.

The reaction of hydration was studied for hydrocarbon $C_6H_8$ (VI). As it is known, vinylacetylenic hydrocarbons with a terminal acetylenic group always add water in accord with the Markovnikov rule with formation of the acetyl grouping. In case of hydrocarbon (VI), on the basis of electronic concepts, one may expect the formation of a mixture of ketones: 4-hexen-3-one (VII) and 4-hexen-5-one (VIII).



$$(VI) \nearrow CH_3CH{=}CH{-}\underset{\underset{O}{\|}}{C}{-}CH_2{-}CH_3 \quad (VII)$$

$$(VI) \searrow CH_3CH{=}CH{-}CH_2{-}\underset{\underset{O}{\|}}{C}{-}CH_3 \quad (VIII)$$

It was shown during the examination of the hydration products that the main reaction product is a ketone with a conjugated system of bonds (VII). This conclusion was drawn on the basis of examination of the absorption curve in the ultraviolet region of the spectrum, since the molar extinction coefficient at the short wave maximum coincided with the literature data for $\alpha,\beta$-unsaturated ketones [10].

## EXPERIMENTAL

Synthesis of isopropylethynylcarbinol (I). Into a three necked flask provided with a propeller stirrer, a reflux condenser and a dropping funnel, there was placed 150 g of powdered potassium hydroxide and 500 ml of absolute ether. A strong stream of acetylene was passed into the ether, with snow cooling, for thirty minutes. To the acetylene-saturated solution (with uninterrupted stream of acetylene) there was added over ten hours drop by drop a solution of 20 g of isobutyraldehyde in 400 ml of absolute ether. The alcoholate was decomposed on the following day by 200 ml of water. The ethereal layer was separated, washed with 2% acetic acid and water. The ethereal layer was dried for one day over calcined potassium carbonate.

B.p. 51° (30 mm), $n^{20}D$ 1.4369, $d^{20}_4$ 0.9291 [11, 12]. $C_6H_{10}F$. Calculated $MR_D$ 29.43. Found $MR_D$ 20.09.

The yield of isopropylethynylcarbinol was 60-65%.

Synthesis of the sulfonate of isopropylethynylcarbinol. To 23.6 g of p-toluenesulfonyl chloride in 12 ml of pyridine there was added dropwise with energetic stirring 11 g of carbinol (I). After completion of the addition of the carbinol the reaction mixture was allowed to stand for 18 hours. After cooling and continued stirring, 15 ml of water was added to the flask, after which the reaction mixture was poured into water. The sulfonate was extracted with ether. The ethereal extract was washed twice with 10% sulfuric acid, with a sodium carbonate solution and with water. The ethereal solution was then dried over sodium sulfate. After the distillation of ether, the sulfonate precipitated in the form of colorless crystals. M.p. 32.5° (from alcohol).

Found %: S 12.09, 12.09. M 260.3. $C_{12}H_{16}O_3S$. Calculated %: S 12.26. M 252.3.

The synthesis of n-propylethynylcarbinol (II) was run under conditions given for the synthesis of isopropylethynylcarbinol. The yield of the carbinol was 60%.

B. p. 87-88° (100 mm), $n^{20}D$ 1.4350, $d^{20}_4$ 0.8710 [11, 12]. $MR_D$ 2935. $C_6H_{12}OF$. Calculated 29.43.

Synthesis of isopropyl(methylethynyl)carbinol (III). To 17 g of magnesium shavings covered with absolute ether there was added dropwise a solution of ethyl bromide (72 g) in double volume of ether. The resulting ethylmagnesium bromide was diluted with a large volume of ether (about 800 ml). Methylacetylene was introduced in 1.5-fold excess, over the calculated amount, into the reaction mixture with ice cooling and energetic stirring. After the reaction mixture had separated into layers, isobutyraldehyde (30 g) was added to the flask. The reaction products were heated at 40° on a water bath and then were allowed to stand for 5-6 days. The organomagnesium complex was carefully decomposed at first with water (50 ml), then with 10% hydrochloric acid. The ethereal solution was neutralized with 10% solution of sodium carbonate, washed with water and dried with potassium carbonate. The yield of the carbinol was 87%.

B.p. 99° (90 mm) [13], $n^{20}D$ 1.4510, $d^{20}_4$ 0.8860, $MR_D$ 34.09. $C_7H_{12}O|\!=$, Calculated 34.05.

Hydrogenation of carbinol (III) was conducted in the presence of platinum black. Carbinol sample: 0.8 g in 25 ml of ethyl alcohol; Pt: 0.08 g. There was absorbed 337.2 ml of hydrogen (0°, 760 mm); the theoretical amount was 320 ml.

Synthesis of ethyl(methylethynyl)carbinol (IV) was run under the conditions which were indicated for the synthesis of carbinol (III).

B.p. 93-94° (90 mm), $n^{20}D$ 1.4508, $d^{20}_4$ 0.8963, $MR_D$ 29.48. $C_6H_{10}O|\!\equiv$. Calculated 29.43.
Found %: C 73.10, 73.35; H 10.35; M 98.75. $C_6H_{10}O$. Calculated %: C 73.42; H 10.27; M 88.14.

Hydrogenation of carbinol (IV) was run in the presence of platinum black. Carbinol sample: 1 g in 25 ml of ethyl alcohol; Pt: 0.1 g. There was absorbed 464.1 ml of hydrogen (0°, 760 mm); theoretical amount: 457.1 ml.

Dehydration of isopropyl(methylethynyl)carbinol. Twenty grams of isopropyl(methylethynyl)carbinol was passed over ten hours in carbon dioxide atmosphere through a tube filled with unglazed porcelain at 300°. The reaction products were collected in a receiver cooled with ice. The hydrocarbon layer was dried with potassium carbonate and distilled in vacuum through a column in a stream of carbon dioxide. There were obtained the following fractions: 1st, b.p. 50-54° (90 mm), 1.4 g, $n^{20}D$ 1.4570; 2nd, b.p. 55-56.5° (90 mm), 4.9 g, $n^{20}D$ 1.4632; 3rd, b.p. 74-79° (90 mm), 6.5 g, $n^{20}D$ 1.4485 (carbinol).

The second fraction corresponds to hydrocarbon (V). The yield of the hydrocarbon was 44%.

Investigation of hydrocarbon (V) $C_7H_{10}$. After second vacuum distillation in carbon dioxide atmosphere the hydrocarbon boiled at 56-57° (90 mm) (see table).

Found %: C 89.55, 89.38; H 10.77, 10.88; M 94.1. $C_7H_{10}$. Calculated %: C 89.29; H 10.70; M 94.15.

Hydrogenation of hydrocarbon (V) was run catalytically in the presence of platinum black. The hydrocarbon sample: 0.8 g in 25 ml of ethyl alcohol; Pt: 0.08 g. There was absorbed 581.8 ml (0°, 760 mm) of hydrogen. The theoretical amount was 571.9 ml.

Oxidation of hydrocarbon (V). To 1.5 g of the hydrocarbon in 100 ml of water there was added, with cooling to 0° and vigorous shaking (the oxidation was run in a flask with a ground-in stopper), crystalline potassium permanganate in small portions until cessation of decolorization. In all 8.4 g of potassium permanganate was added, instead of 9.4 g required theoretically. After completion of addition of potassium permanganate, the manganese dioxide was filtered off, washed on the filter with hot water and the neutral products were distilled from the filtrate. The distillate was utilized for the preparation of p-nitrophenylhydrazone while acetone was determined quantitatively in a separate portion by the hydroxylamine method. The p-nitrophenylhydrazone, recrystallized from alcohol, melted at 148° and gave no depression in mixture with the p-nitrophenylhydrazone of acetone. It was established by oximation that 10 ml of the aliquot sample contained 0.04 g of acetone. On recalculation to the entire solution, the acetone content in the oxidation products was found to be 0.4 g (44%).

The volatile acids were distilled from the acidified solution of the salts. The acids were titrated with 0.1 N solution of sodium hydroxide; 120 ml of 0.1 N sodium hydroxide was required for the titration, which amount corresponded to 0.72 g (75%) of acid, as calculated in terms of acetic acid. The solution of the salts of volatile acids after the neutralization was concentrated to a volume of 40-50 ml. After acidification the acids were distilled into a flask with freshly prepared silver carbonate. The resulting silver salts corresponded to the silver salt of acetic acid in their composition.

Found %: C 14.61, 14.58; H 2.12, 2.08; Ag 65.04, 64.91. $C_2H_3O_2Ag$. Calculated %: C 14.36; H 1.94; Ag 64.66.

The nonvolatile acids were extracted in an extractor. Oxalic acid (m.p. 102°) was isolated in an insignificant amount. The acid was identified by mixed melting point with an authentic specimen.

Ozonolysis of hydrocarbon (V). The ozonolysis was run for the quantitative determination of formaldehyde and formic acid. If the hydrocarbon had contained a considerable admixture of the isomeric hydrocarbon with a terminal methylene group, the ozonolysis products should have contained formaldehyde and formic acid. The ozonolysis was run in chloroform in A. I. Iakubchik's apparatus. The amount of formaldehyde, determined through formaldehyde derivative of dimethylcyclohexanedione, was 0.47% (calculated for the ozonide). The amount of formic acid (determined by the calomel method) was 1.1% (calculated on the ozonide). Such insignificant amounts of formaldehyde and formic acid are always contained in ozonolysis products; therefore the hydrocarbon (V) does not contain the admixture of a hydrocarbon with a terminal methylene group.

The spectrum in the infrared region was determined for the hydrocarbon (V) on the IKS-11 spectrometer. The layer thickness was 0.05 mm; sodium chloride prism was used (see figure).

Dehydration of ethyl(methylethynyl)carbinol. Forty grams of ethyl(methylethynyl)carbinol was passed over 15 hours through a tube filled with magnesium sulfate at 270°. The dehydration was run in an atmosphere of nitrogen. The reaction products were collected in a receiver cooled with ice. The hydrocarbon layer was dried with potassium carbonate and distilled in vacuum in nitrogen atmosphere. There were collected the following fractions: 1st, b.p. 18-35° (90 mm), 0.8 g, $n^{20}D$ 1.4570; 2nd, b.p. 35.5-36.5° (90 mm), 9.2 g, $n^{20}D$ 1.4630 (hydrocarbon); 3rd, b.p. 38-40° (90 mm), 0.9 g, $n^{20}D$ 1.4580; 4th, b.p. 83-92° (90 mm), 14.5 g, $n^{20}D$ 1.4505 (carbinol). The yield of the hydrocarbon fraction was 44% based on the reacted carbinol.

Investigation of hydrocarbon $C_6H_8$ (VI). After second distillation in vacuum in nitrogen atmosphere the hydrocarbon had the following properties: b.p. 91-92° (760 mm), 35.5-36.5° (90 mm) (see table).

Found %: C 89.76, 89.62; H 10.17, 10.16. M 79.4. $C_6H_8$. Calculated %: C 89.95; H 10.06; M 80.13.

The spectrum of hydrocarbon (VI) was determined in the infrared region by means of IKS-11 spectrometer. Lithium fluoride and sodium chloride prisms were used. The layer thickness was 0.05 mm (see figure).

Hydrogenation of hydrocarbon (VI) was run catalytically in the presence of platinum black. The hydrocarbon sample: 1.0 g; Pt: 0.7 g. There was absorbed 840.0 ml of hydrogen (0°, 760 mm); theoretical amount was 839.7 ml.

Hydration of hydrocarbon $C_6H_8$ (VI). Into a three-necked flask, provided with a stirrer, a reflux condenser, thermometer and a dropping funnel, there was placed 180 ml of water, 7 ml of concentrated sulfuric acid, 3 g of mercuric oxide and 10 ml of 50% solution of $Fe_2(SO_4)_3$. The reaction mixture was heated to 70°, after which 9 g of the hydrocarbon was added to it dropwise. After the addition of the hydrocarbon, the reaction mixture was heated for two and a half hours longer at 70-75°.

The ketone was distilled in vacuum in nitrogen atmosphere. There were obtained the following fractions: 1st, b.p. 69° (90 mm), 0.3 g, $n^{20}D$ 1.4368; 2nd, b.p. 74.5-76.5° (90 mm), 4.7 g, $n^{20}D$ 1.4386 (ketone); flask residue: 0.5 g. The yield of the ketone fraction was 48%.

Investigation of the second fraction.

B.p. 74.5-76.5° (90 mm), $n^{20}D$ 1.4386, $d^{20}_4$ 0.8580 [14]; $MR_D$ 30.12. $C_6H_{10}O$F. Calculated 29.45.
Found %: C 73.24, 73.48; H 10.58, 10.61. $C_6H_{10}$. Calculated %: C 73.42; H 10.27.

The absorption curve was taken for this fraction, by means of the SF-4 spectrophotometer. Ethyl alcohol was used as the solvent (c = 0.00466-0.00003 ml). Wavelength of absorption maximum was 224 mμ, log $\epsilon$ 4.13; another maximum at 310 mμ, log $\epsilon$ 1.57.

2,4-Dinitrophenylhydrazone was prepared from the ketone. The hydrazone thus prepared was red and contained an insignificant admixture of yellow crystals. M.p. 95-106°.

Found %: N 20.24, 20.39. $C_{12}H_{14}O_4N_4$. Calculated %: 20.13.

## SUMMARY

1. A method of synthesis of secondary acetylenic alcohols by the A. E. Favorskii method was worked out.

2. It was shown that secondary $\alpha,\beta$-acetylenic alcohols with a terminal acetylenic group do not lose water under conditions which are usual for the dehydration of tertiary $\alpha,\beta$-acetylenic alcohols.

3. There were prepared and characterized two enyne hydrocarbons: 2-methyl-2-hexen-4-yne and 2-hexen-4-yne, which were obtained by the dehydration of isopropyl(methylethynyl)carbinol and the ethyl (methylethynyl) carbinol which was synthesized for the first time.

4. It was shown spectroscopically that hydration of 2-hexen-4-yne leads mainly to the formation of the α,β-unsaturated ketone 4-hexen-3-one.

## LITERATURE CITED

[1] I. A. Favorskaia, Iu. P. Artsybasheva and L. V. Fedorova, J. Gen. Chem. 27, 1490 (1957).*

[2] G. Eglinton and M. C. Whiting, J. Chem. Soc. 3650 (1950).

[3] W. F. Anzilotti and R. R. Vogt, J. Am. Chem. Soc. 61, 572 (1939).

[4] G. H. Jeffery, and A. J. Vogel, J. Chem. Soc. 1948, 674.

[5] B. V. Ioffe, J. Anal. Chem. USSR 4, 183 (1949).

[6] N. Sheppard, J. Chem. Phys. 17, 75 (1949).

[7] J. L. H. Allan, G. D. Meakins and M. C. Whiting, J. Chem. Soc. 1955, 1874.

[8] A. Weisberger, Chemical Application of Spectroscopy, 368 (1956).

[9] E. Bergman and D. Sprinzak, J. App. Chem. 3, 97 (1953).

[10] J. M. Bonmer and G. Gandemaris, Bull. Soc. Chim. 1954, 997.

[11] Iu. S. Zal'kind and I. M. Gvartsiteli, J. Gen. Chem. 9, 971 (1939).

[12] I. N. Nazarov and L. Kotliarevskii, J. Gen. Chem. 23, 1900 (1953).*

[13] Zh. I. Iotsich, J. Russ. Chem. Soc. 41, 529 (1909).

[14] P. S. Stutsman and H. Adkins, J. Am. Chem. Soc. 61, 3306 (1939).

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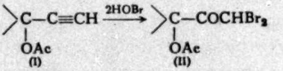
# THE SIMPLEST ANALOGS OF CORTICOSTEROIDS

## II. INTRODUCTION OF DIHYDROXYCARBOXYLIC, GLYCERYL AND HYDROXYACETONE SIDE CHAINS INTO o-METHYLCYCLOHEXANONE AND THE STEREOCHEMISTRY OF THE COMPOUNDS FORMED THEREBY

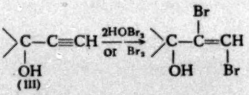
I. N. Nazarov and A. A. Akhrem

Introduction of the dihydroxyacetone side chain into cyclic compounds is of considerable interest in connection with the problem of the total synthesis of cortisone and its simplest analogs. The absence of satisfactory methods of introduction of the dihydroxyacetone side chain into steroidal ketones forces organic chemists to seek some new paths to the solution of this important problem. Several years ago we used for this purpose [1] the reaction of addition of hypobromous acid to the triple bond, reaction discovered by Favorskii [2], with its employment among the readily preparable acetylenic alcohols and their acetates.

As it turned out in the case of acetates of tertiary acetylenic alcohols (I), the reaction of addition of hypobromous acid to the triple bond proceeded normally and led to the preparation of the corresponding acetates of the dibromoketols (II), while in the case of alcohols (III) there occurred the addition of two atoms of bromine to the triple bond.



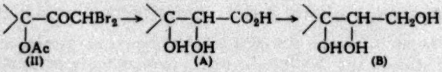
$$\underset{\text{(I)}}{\underset{\text{OAc}}{>\text{C}}}-\text{C}\equiv\text{CH}\xrightarrow{\text{2HOBr}}\underset{\text{(II)}}{\underset{\text{OAc}}{>\text{C}}}-\text{COCHBr}_2$$



$$\underset{\text{(III)}}{\underset{\text{OH}}{>\text{C}}}-\text{C}\equiv\text{CH}\xrightarrow[\text{or Br}_2]{\text{2HOBr}_2}\underset{\text{OH}}{>\text{C}}-\overset{\text{Br}}{\text{C}}=\underset{\text{Br}}{\text{CH}}$$

The same regularity is observed in the case of addition of hypobromous acid to the vinyl analogs of compounds (I) and (III).

We observed an intramolecular rearrangement during the reaction of barium hydroxide with the acetates of dibromoketols (II), this rearrangement leading to the formation of the corresponding dihydroxycarboxylic acids (A) which may be reduced with lithium aluminum hydride to the corresponding triols (B), which are important intermediates in the synthesis of the dihydroxyacetone side chain.



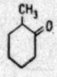
$$\underset{\text{(II)}}{\underset{\text{OAc}}{>\text{C}}}-\text{COCHBr}_2\rightarrow\underset{\text{OH}}{>\text{C}}-\underset{\text{(A)}}{\underset{\text{OH}}{\text{CH}}}-\text{CO}_2\text{H}\rightarrow\underset{\text{OH}}{>\text{C}}-\underset{\text{OH}}{\text{CH}}-\underset{\text{(B)}}{\text{CH}_2\text{OH}}$$

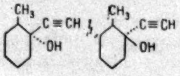
The absence of asymmetric centers in the acetylenic alcohols, previously described by us [1], did not permit us to study the stereochemistry of these interesting reactions.

We selected the accessible o-methylcyclohexanone (IV), in the molecule of which there exists one asymmetric center, for the simplest model compound with which one may study the stereochemistry of the introduction of a side chain into cyclic compounds.

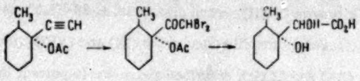
The results of our studies are presented in this communication.

Two epimeric acetylenic alcohols: crystalline (V) and liquid (VI), are formed in the condensation of o-methylcyclohexanone (IV) with acetylene under pressure [3] in the presence of powdered potassium hydroxide. Here the quantitative ratio of the epimers (V) and (VI) depend, evidently, on the conditions used for the experiment. Thus, in the synthesis run in liquid ammonia [4] there is formed 33% of (V) and 66% of (VI), while under the Favorskii reaction conditions the yield of the crystalline isomer (V) reaches 60%. The formation of two epimers (V) and (VI) has been observed previously [5], but only rather recently [4] were these isolated in the pure state. However, their geometric configuration has not been determined until the present. Recently we [6] related the epimeric acetylenic alcohols (V) and (VI) to the known pair of cis- and trans-1,2-dimethylcyclohexanols [7], and thereby showed that the crystalline 1-ethynyl-2-methylcyclohexanol (V) corresponds to the cis-disposition of the methyl and the ethynyl groups, while the liquid epimer (VI) corresponds to the trans-disposition of these groups. This result is also confirmed by the data obtained previously [8] on the behavior of dienes synthesized from epimeric alcohols (V) and (VI) in the reaction of diene synthesis.


(IV)

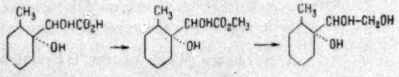

(V) (VI)

The acetate of cis-1-ethynyl-2-methylcyclohexanol (VII) was prepared in high yield during the acetylation of alcohol (V) by excess acetic anhydride. By the action of hypobromous acid on the latter there is obtained, in 95% yield, the crystalline acetate of cis-1(ω-dibromoacetyl)-2-methylcyclohexanol (VIII).


(VII) (VIII) (IX) (X)

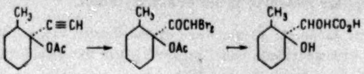
The intramolecular rearrangement, described by us earlier [1], takes place during the action of an aqueous solution of barium hydroxide on the acetate of the cis-dibromoketol (VIII), and during this reaction there is formed, in yield of about 50%, the mixture of the two isomeric dihydroxycarboxylic acids (IX) and (X), with melting points 149-150° and 128.5-129°, respectively, which are predicted by theory and which differ from each other in the configuration of the secondary hydroxyl.

The acid (IX) is formed in greatly predominant amount. Its methyl ester (XI) is formed by the action of an ethereal solution of diazomethane on acid (IX) and the reduction of this ester with lithium aluminum hydride led to the formation, in high yield, of the triol (XII) with melting point 88-88.5°.

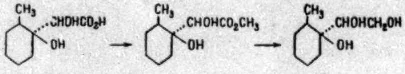

(IX) (X) (XI), Liquid (XIII) (XII) (XIV)

Acid (X) gave, under these conditions, a crystalline methyl ester (XIII) with m.p. 73-74° on the reduction of which with lithium aluminum hydride there was formed, in 50% yield, the triol (XIV), with m.p. 90-90.5°, which was epimeric to triol (XII) at the secondary hydroxyl group. The mixed melting point of the isomeric triols (XII) and (XIV) shows a large depression and melts at 50-55°.

Analogous transformations were also realized with the liquid transacetylenic alcohols (VI). Its acetate (XV) was prepared by acetylation of the latter, and, by the action of hypobromous acid on this acetate, there was formed in 95% yield the acetate of trans-1( ω-dibromoacetyl)-2-methyl-cyclohexanol (XVI).


(XV) (XVI) Liquid (XVII)
(XVIII)

The intramolecular rearrangement, which leads to the formation, in 50% yield, of a second pair of dihydroxy-carboxylic acids (XVII) and (XVIII), with melting points 156-156.5° and 109.5-110°, respectively, which are epimeric at the secondary hydroxyl, again takes place during the hydrolysis of the acetate of the dibromoketol (XVI) with barium hydroxide. Again in this case the high-melting acid (XVII) was isolated in the predominant amount. Thus, the intramolecular rearrangement of the acetate of dibromoketols (VIII) and (XVI) does not proceed stereospecifically. The methyl ester (XIX), with m.p. 91-91.5°, of the high-melting acid (XVII) was prepared by the action of an ethereal solution of diazomethane on the acid; the reduction of this ester with lithium aluminum hydride gave the triol (XX), with m.p. 125-125.5°, in high yield.

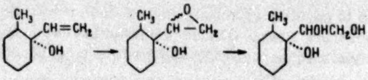

(XVII) (XIX) (XX)
(XVIII) (XXI) (XXII)

Trans-acid (XVIII) under these conditions gave its methyl ester (XXI) with m.p. 53-54°, on the reduction of which with lithium aluminum hydride there was obtained triol (XXII), with m.p. 88-88.5°, in 50% yield. The reaction gave directly a triol with m.p. 76-78° (from ether) and a small amount of crystals with m.p. 88-88.5°. Its mixed melting point with a sample of XII), which also melts at 88-88.5°, gave m.p. 55-65°.

Attempts to prepare acetonates of the dihydroxy acids (IX) and (XVII) turned out to be fruitless.

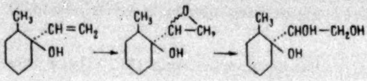
The triols (XII), (XIV), (XX) and (XXII), described above, are important intermediates in the synthesis of the dihydroxyacetone side chain. For their preparation we also used the glycidic method described by us previously [1].

Selective catalytic hydrogenation of the cis-acetylenic alcohol (V) over palladium catalyst gave, in high yield, the cis-1-vinyl-2-methyl-cyclohexanol (XXIII), the oxidation of which with peracetic acid, by the Prilezhaev method, in chloroform gave 80% yield of a mixture of isomeric glycidic alcohols (XXIV) in the form of crystals and a liquid oil.


(XXIII) (XXIV) (XII)
(XIV)

The crystalline glycidol (XXIV), formed in the greater amount, is hydrolyzed, on heating with acidified water, to triol (XII), in good yields, this triol having been also obtained, as indicated above, from the high-melting isomer of the cis-acid (IX), which was also formed in a predominant amount.

The liquid glycidol (XXIV) gave on hydrolysis a certain amount of a difficultly crystallizable thick sirup from which there was isolated a small amount of crystals of triol (XIV) which did not give a mixed melting point depression with the specimen, described above, which was prepared by reduction of acid (X). On selective hydrogenation of trans-1-ethynyl-2-methylcyclohexanol (VI) there was formed trans-1-vinyl-2-methylcyclohexanol (XXV), the oxidation of which with peracetic acid led to the preparation of glycidic alcohols (XXVI), isolated in the form of two crystalline isomers with m.p. 41° and 75°. The high-melting isomer was isolated in the predominant amount.

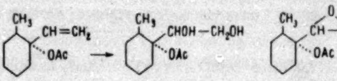

(XXV) (XXVI) (XX) (XXVII)

Hydrolysis of the low-melting isomer (XXVI) gave the triol (XXII), with m.p. 88.5°, synthesized by us by the reduction of the low-melting acid (XVIII). The above-described triol (XX), synthesized by the reduction of the high-melting acid (XVII), was obtained on hydrolysis of the high-melting glycidol (XXVI).

As it is evident from the experimental results, the oxidation of vinyl alcohols (XXIII) and (XXV) with peracetic acid proceeds unselectively and leads to the formation of all possible isomers of the glycidic alcohols (XXIV) and (XXVI) with different configurations of the oxide ring.

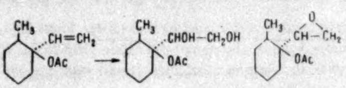
In the selective catalytic hydrogenation over palladium catalyst of the cis-acetate (VII) there was formed the acetate of cis-2-methyl-1-vinyl-1-cyclohexanol (XXVIII); the trans-acetate (XV), under these conditions, gave the acetate of trans-2-methyl-1-vinyl-1-cyclohexanol (XXIX).

In oxidation of the acetate (XXVIII) with peracetic acid there was formed the mixture of two epimeric monoacetates of triols (XXX) and (XXXI). The normal oxidation products – acetates of glycidic alcohol (XXXII) – were not isolated in this reaction.


(XXVIII) (XXX) (XXXI) (XXXII)

It was shown by alkaline hydrolysis of acetates (XXX) and (XXXI) that they contain one acetyl group. In this reaction, from the hydrolysis products of acetate (XXX) there was isolated the above-described triol (XII). Acetate (XXXI) gave the above-described triol (XIV) on hydrolysis.

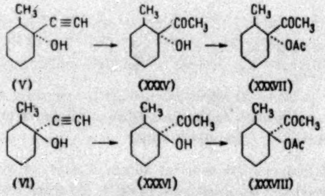
A similar result was obtained in oxidation of the trans-acetate (XXIX).


(XXIX) (XXXIV) (XXXIII)

In this case, instead of the expected acetate of the glycidic alcohol (XXXIII), there was isolated a liquid mixture of acetates of isomeric triols (XXXIV), on the hydrolysis of which there were obtained the above-described triol (XXIII) and an unknown triol (XXXVII), with m.p. 112°. Triol (XVII) was obtained in the greater amount. These results testify that the oxidation of acetates of tertiary vinyl alcohols with peracetic acid, in contrast to the oxidation of the corresponding vinyl alcohols and acetates of allylic alcohols, proceeds differently and does not lead to the formation of normal oxidation products – acetates of glycidic alcohols [1]. Theory predicts for the epimeric pair of vinyl alcohols (XXIII) and (XXV) the possibility of formation of four racemic triols (three asymmetric centers exist in the molecule). We isolated three crystalline triols (XX), (XXII), and (XXVII) in the trans-series. This result testifies that there takes place here, evidently, a phenomenon of polymorphism or the formation of mixed crystals of (XXVII) with m.p. 112°.

Conformational analysis permits one to connect, as it is known, the stereochemistry of a molecule with its reactivity [9]. Therefore it was of interest to study the reaction of hydration of the triple bond on the examples of the pair of epimeric acetylenic alcohols (V) and (VI), as well as to study the acetylation of the tertiary hydroxyl with the purpose of establishment of the dependence of the reaction rate on the equatorial or the axial disposition of the substituent. On hydration of cis-alcohol (V) in methanolic solution in the presence of mercuric sulfate and sulfuric acid, there was formed in almost quantitative yield the cis-α-ketol (XXXV) with m.p. 37-38°, which had been prepared earlier [4].

Trans-alcohol (VI) hydrates into liquid trans-α-ketol (XXXVI) at a somewhat greater rate but in lower yield.



A greater distinction is observed in the reaction of acetylation of the hydroxyl group in the epimeric pair of α-ketols (XXXV) and (XXXVI). In case of cis-α-ketol (XXXV) the acetylation proceeds under mild conditions by refluxing with excess acetyl chloride in ether. Under these conditions the trans-α-ketol (XXXVI) does not acetylate at all. We failed to esterify it under even more drastic conditions – with acetyl chloride in pyridine. Only by the action of acetic anhydride in the presence of concentrated sulfuric acid could acetylation of the hydroxyl in trans-α-ketol (XXXVI) be made to take place. The yields of acetates (XXXVII) and (XXXVIII) were close to the theoretical.

This result testifies that in the cis-α-ketol (XXXV) the tertiary hydroxyl is evidently in the equatorial configuration, while in the trans-α-ketol (XXXVI) it has the axial position [9, 10].

## EXPERIMENTAL

Acetate of cis-2-methyl-1-ethynyl-1-cyclohexanol (VII). A solution of 200 g of cis-alcohol (V) (m.p. 56-57°) and 300 g of freshly distilled acetic anhydride was refluxed for three hours. After cooling, the excess acetic anhydride was distilled off in vacuum, the residue was dissolved in ether, neutralized with a sodium bicarbonate solution and dried with sodium sulfate. There was obtained 207 g of the acetate of cis-2-methyl-1-ethynyl-1-cyclohexanol (VII) in the form of a colorless liquid with b.p. 102-103° (15 mm), $n^{18}D$ 1.4675.

Acetate of trans-2-methyl-1-ethynyl-1-cyclohexanol (XV). From 250 g of alcohol (VI) and 1000 g of acetic anhydride there was obtained, under the above-described conditions, 255 g, of the acetate of trans-2-methyl-1-ethynyl-1-cyclohexanol (XV) in the form of a colorless liquid with b.p. 98-102° (18 mm), $n^{19}D$ 1.4650.

Acetate of cis-2-methyl-1(ω-dibromoacetyl)-1-cyclohexanol (VIII). To the aqueous solution of bromoacetamide [1], obtained from 60 g of acetamide and 150 g of bromine in 300 ml of water, there was added 50 g of sodium acetate and 30 ml of glacial acetic acid, after which there was added 35 g of acetate (VII). The temperature of the reaction mixture was kept from rising above 25° by suitable cooling. After two hours, the precipitated reaction product was separated and dissolved in ether. The ethereal solution was neutralized with sodium bicarbonate and dried with sodium sulfate. There was obtained 70 g of crystals from which there was isolated, after crystallization from petroleum ether, 62 g of cis-dibromoketol (VIII) in the form of colorless crystals with m.p. 90-90.5°.

Found %: C 37.24, 37.06; H 4.34, 4.40; Br 45.06, 45.37. $C_{11}H_{16}O_3Br_2$. Calculated %: C 37.10; H 4.49; Br 44.64.

Rearrangement of the acetate of cis-dibromoketol (VIII). Preparation of cis-dihydroxycarboxylic acids: cis-2-methyl-1-hydroxycyclohexylglycolic acids (erythro-threo isomerism) (IX) and (X). To the solution of 120 g of barium hydroxide in 200 ml of water there was added dropwise at 70-75° and with energetic stirring a solution of 58 g of cis-dibromoketol (VIII) in 150 ml of trimethylcarbinol. A rise in the temperature of the reaction mixture was observed (to 80-85°), this temperature being maintained for 5-7 minutes despite cooling the reaction flask with cold water. After cooling, the solution was filtered, the filtrate was evaporated to dryness in vacuum and the residue was extracted with ether to remove the neutral products. Then the residue was treated with 15% hydrochloric acid and the precipitated acids were extracted with ether. There was obtained 7 g of liquid products and 12.5 g of crystals, which after fractional recrystallization from ether, petroleum ether and iso-octane, gave two isomeric cis-dihydroxycarboxylic acids (IX) and (X). The dihydroxy acid (IX), which formed colorless crystals with m.p. 149.5-150° (from ether) was isolated in the predominant amount.

Found %: C 57.42, 57.64; H 8.51, 8.62. $C_9H_{16}O_4$. Calculated %: C 57.45; H 8.51.

The dihydroxy acid (X), which was isolated in a small amount, melted at 128.5-129° (from ether).

Found %: C 57.64, 57.53; H 8.44, 8.42. $C_9H_{16}O_4$. Calculated %: C 57.45; H 8.51.

The mixed melting point of acids (IX) and (X) was 102-120°. These acids form a difficultly separable mixture with a stable m.p. 117-118° (from chloroform).

Acetate of trans-2-methyl-1(ω-dibromoacetyl)-1-cyclohexanol (XVI). By the action of an aqueous solution of bromoacetamide, prepared as shown above from 85 g of acetamide and 220 g of bromine in 300 ml of water, on 60 g of acetate (XV) (b.p. 98-102° at 18 mm) there was obtained 116 g of trans-dibromoketol (XVI) in the form of nearly colorless viscous oil with b.p. 152-153° (3 mm), $n^{20}D$ 1.5275.

Found %: C 36.93, 36.82; H 4.27, 4.38; Br 44.83, 44.69. $C_{11}H_{16}O_3Br_2$. Calculated %: C 37.10; H 4.49; Br 44.64.

Rearrangement of the acetate of trans-dibromoketol (XVI). Preparation of trans-dihydroxy carboxylic acids: trans-2-methyl-1-hydroxycyclohexyl-glycolic acids (erythro-threo isomerism) (XVII) and (XVIII). By hydrolysis of 70 g of the acetate of trans-dibromoketol (XVI) with barium hydroxide under conditions described above there was isolated 18 g (the yield was about 50% of the isomeric mixture) of two isomeric trans-dihydroxy carboxylic acids – (XVII) and (XVIII). The dihydroxy acid (XVII), which was isolated in the predominant amount, melted at 156-156.5° (from ether).

Found %: C 57.46, 57.28; H 8.63, 8.65. $C_9H_{16}O_4$. Calculated %: C 57.45; H 8.51.

Dihydroxy acid (XVIII) melted at 109.5-110° (from chloroform).

Found %: C 57.60, 57.58; H 8.56, 8.36. $C_9H_{16}O_4$. Calculated %: C 57.45; H 8.51.

Acids (XVII) and (XVIII) form a difficultly separable mixture with a stable m.p. 103-104° (from chloroform). Mixed melting point of these acids melted at 102-133°.

Methyl ester of the cis-dihydroxy acid (XI). To a solution of 2 g of cis-dihydroxy acid (IX) (m.p. 149.5-150°) in 100 ml of ether there was added the ethereal solution of diazomethane prepared from 16 g of nitrosomethylurea. On the following day, after distillation of ether, there was obtained about 2 g of the methyl ester of (XI) in the form of a viscous colorless oil which was subjected to reduction without further purification.

Reduction of methyl ester (XI) with lithium aluminum hydride to the triol – cis-2-methyl-1-hydroxycyclohexyl glycol (m.p. 88°) (XII). Into a three-necked flask provided with a mechanical stirrer, a reflux condenser, a calcium chloride tube and a dropping funnel, there was placed 1 g of lithium aluminum hydride in 200 ml of absolute ether (a suspension) and to this there was added from the dropping funnel with continued stirring over ten minutes an ethereal solution of 1 g of methyl ester (XI). Then the reaction mixture was refluxed for three hours and allowed to stand overnight at room temperature. On the following day 5 ml of ethyl acetate was added with cooling and the product was treated with 20 ml of 10% sulfuric acid, extracted with ether, washed with a solution of sodium bicarbonate and dried with sodium sulfate. After distillation of ether there was obtained 0.9 g of a sirup, which crystallized after addition of ether. Recrystallization from a mixture of ether with petroleum ether gave 0.6 g of triol (XII) with m.p. 88-88.5°. Some 0.3 g of crystals of the triol was obtained in addition from the mother liquor.

Found %: C 62.06, 62.07; H 10.23, 10.33. $C_9H_{18}O_3$. Calculated %: C 62.07; H 10.35.

Methyl ester (XIII). By the action of an ethereal solution of diazomethane there was obtained from 0.09 g of acid (X) (m.p. 128.5-129°) 0.05 g of methyl ester (XIII) in the form of prisms with m.p. 73-74° (from petroleum ether).

Reduction of methyl ester (XIII) with lithium aluminum hydride into triol – cis-2-methyl-1-hydroxycyclohexyl glycol (m.p. 90°) (XIV). By the reduction of 0.05 g of methyl ester (XIII) with m.p. 73-74° with lithium aluminum hydride, as described above (refluxing for seven hours) there was obtained 0.02 g of crystals with m.p. 82-87° (from iso-octane). After repeated crystallization from iso-octane there was isolated the triol (XIV) with m.p. 90-90.5°.

Found %: C 61.72, 61.85; H 10.33, 10.36. $C_9H_{18}O_3$. Calculated %: C 62.07; H 10.35.

The mixed melting point with isomeric triol (XII) was 50-55°.

Methyl ester of trans-acid (XIX). From 2 g of trans-acid (XVII) (m.p. 156-156.5°) there was obtained by the action of an ethereal solution of diazomethane 1.9 g of methyl ester (XIX) in the form of colorless needles with m.p. 91-91.5° (ether + petroleum ether).

Found %: C 59.37, 59.23; H 8.92, 8.86. $C_{10}H_{18}O_4$. Calculated %: C 59.41; H 8.91.

Reduction of methyl ester (XIX) to the triol: trans-2-methyl-1-hydroxycyclohexyl glycol (m.p. 125°). Methyl ester (XIX) (0.85 g) was reduced with a four-fold excess of lithium aluminum hydride as described above. There was obtained 0.6 g of the triol (XX) in the form of colorless prisms with m.p. 125-125.5°.

Found %: C 61.67, 61.75; H 10.30, 10.36. $C_9H_{18}O_3$. Calculated %: C 62.07; H 10.35.

From the mother liquor there was isolated an additional 0.1 g of the triol (XX) with m.p. 120-123°.

Methyl ester of trans-acid (XXI). By the action of diazomethane, as described above, there was prepared from 0.4 g of trans-acid (XVIII) (m.p. 109.5-110°) 0.4 g of methyl ester (XXI) with m.p. 53-54° (from iso-octane). The entire amount of the methyl ester was used for the reduction.

Reduction of methyl ester (XXI) into triol: (trans-2-methyl-1-hydroxycyclohexyl glycol (m.p. 88.5°) (XXII). By reduction of 0.4 g of methyl ester (XXI) (m.p. 53-54°) by a four-fold excess of lithium aluminum hydride, as described above (refluxed for nine hours) there was obtained about 0.2 g of crystals with m.p. 76-78° and 0.05 g of crystals with m.p. 86-87° (rhombic plates). A mixed melting point of the two was 77-79°. After recrystallization from a mixture of ether and petroleum ether of the crystals with m.p. 76-78° there was obtained 0.1 g of triol (XXII) with the same melting point. An additional recrystallization from high-boiling petroleum ether, with preliminary melting of the sample, gave crystals with m.p. 88-88.5° (needles).

Found %: C 62.24, 62.13; H 10.46, 10.24. $C_9H_{18}O_3$. Calculated %: C 62.07; H 10.35.

Triol (XXII) gave a large depression in mixed melting points with the triols prepared above (XII) and (XIV) with m.p. respectively, 88-88.5° and 90-90.5° (the mixed melting points were 55-65° and 50-62°).

Preparation of cis-1-vinyl-2-methyl-1-cyclohexanol (XXIII). Cis-acetylenic alcohol (V) (220 g) (m.p. 56-57°) was hydrogenated in 100 ml of methanol over 2.5 hours under hydrogen pressure of 4 atm in a reactor with a stirrer in the presence of 0.25 g of $Pd/CaCO_3$ (about 5% palladium) until the calculated amount of hydrogen was absorbed (38 l). The end of hydrogenation was controlled by an acetylenic test. There was obtained 219 g of the vinyl alcohol (XXIII) [8] in the form of a colorless liquid with b.p. 87-87.5° (21 mm), $n^{21}D$ 1.4767.

Cis-1-ethyl-2-methyl-1-cyclohexanol was obtained in the form of a colorless liquid with b.p. 76-76.5° 11.5 mm), $n^{19}D$ 1.4712 [11] after exhaustive hydrogenation of acetylenic alcohol (V).

Synthesis of trans-1-vinyl-2-methyl-1-cyclohexanol (XXV). On hydrogenation of 304 g of liquid acetylenic trans-alcohol (VI) (b.p. 75° at 15 mm, $n^{19}D$ 1.4770) in the presence of 0.33 g of palladium catalysts, analogously to above, (the hydrogenation was interrupted after absorption of 53 liters of hydrogen) there was obtained after a vacuum distillation 280 g of trans-vinyl alcohol (XXV) in the form of a colorless liquid with b.p. 65-67° (8 mm), $n^{22}D$ 1.4720.

On exhaustive hydrogenation of acetylenic alcohol (VI) there was obtained trans-1-ethyl-2-methyl-1-cyclohexanol in the form of a colorless liquid with b.p. 71-72° (11 mm), $n^{19}D$ 1.4683.

Oxidation of cis-vinyl alcohol (XXIII) with peracetic acid. To the solution of 20 g of vinyl alcohol (XXIII) (b.p. 87-87.5° at 21 mm, $n^{21}D$ 1.4767) in 100 ml of chloroform there was added 13.5 g of 90% peracetic acid (10% excess). The reaction temperature was maintained at 20° with water cooling. After four hours there formed an upper layer of a colorless liquid. The oxidation reaction was completed after three days. At this time there remained in the reaction mixture some 2.4 g of peracetic acid (the added excess was 1.8 g). The solution was neutralized with aqueous sodium bicarbonate and dried with sodium sulfate. After vacuum distillation there was obtained 19.5 g of a colorless liquid with b.p. 88-91° (6 mm), $n^{14}D$ 1.4757, which consisted of a mixture of glycidic alcohols. After prolonged freezing of the mixture we succeeded in isolating some 10 g of the glycidol (XXIV) with m.p. 43-43.5° (from petroleum ether).

Found %: C 69.00, 69.12; H 10.16, 10.10. $C_9H_{16}O_2$. Calculated %: C 69.87; H 10.26.

As the result of fractional vacuum distillation there was obtained from the liquid portion, amounting to 8 g, some liquid glycidol (XXIV).

B.p. 89-90° (7 mm), $n^{20}D$ 1.4780, $d^{20}_4$ 1.0389. $MR_D$ 42.50. Calculated 42.53 (without the oxide ring increment).

Found %: C 68.90, 69.03; H 10.26, 10.42. $C_9H_{16}O_2$. Calculated %: C 69.23; H 10.26.

In iodometric determination of the unreacted peracetic acid in this experiment there was isolated a substance with m.p. 115-116° (decomposition)(from ether + petroleum ether), which was the product of addition of hydroiodic acid to the glycidic alcohol.

Found %: C 37.95, 38.09; H 6.09, 6.08; I 44.67, 44.75. $C_9H_{17}O_2I$. Calculated %: C 38.04; H 5.98; I 44.70.

Oxidation of trans-vinyl alcohol (XXV) with peracetic acid. On oxidation of 20 g of trans-vinyl alcohol (XXV) with peracetic acid, as described above, there was obtained 20 g of a colorless, viscous, partly crystallizable liquid, from which, after repeated freezing, there was isolated 10 g of crystalline glycidol (XXVI) with m.p. 75-75.5° (from petroleum ether).

Found %: C 69.25, 69.50; H 10.49, 10.46. $C_9H_{16}O_2$. Calculated %: C 69.23; H 10.26.

Mixed melting point with glycidol (XXIV) (m.p. 43°) was 35-37°.

After separation of the crystals with m.p. 75° from the liquid reaction product and a vacuum distillation through a column there was obtained 2 g of low-melting glycidol (XXVI) in the form of a colorless viscous oil.

B.p. 86-87° (7 mm), $n^{20}D$ 1.4715, $d^{20}_4$ 1.0253. $MR_D$ 42.57; calculated 42.53 (without the oxide ring increment). M.p. 40.5-41° (petroleum ether).

Found %: C 69.37, 69.51; H 10.30, 10.41. $C_9H_{16}O_2$. Calculated %: C 69.23; H 10.26.

After prolonged standing of the liquid glycidol there was observed some crystallization with formation of crystals of glycidol (XXVI) with m.p. 40.5-41°. Mixed melting point with the high-melting glycidol (m.p. 75°) was 35-36°. Mixed melting point with (XXIV) (m.p. 43.5°) was 20°.

Hydrolysis of crystalline cis-2-methyl-1-hydroxycyclohexylethylene oxide (m.p. 43°) (XXIV) into triol (XII). Cis-glycidol (XXIV) with m.p. 42.5-43° (0.53 g) in 100 ml of distilled water containing 2 ml of glacial acetic acid was refluxed for three hours. After filtration the solution was evaporated in vacuum, leaving as a residue 0.6 g of a viscous sirup on recrystallization of which from a mixture of ether and petroleum ether there was isolated 0.3 g of triol (XII) with m.p. 88-88.5°, which did not give a depression in mixed melting point with the specimen prepared above. In addition to the crystals there was obtained in this experiment some 0.25 g of an uncrystallizable sirup. The liquid glycidol (XXIV) under these conditions gave a viscous, difficultly recrystallizing sirup, from which there was isolated, in a small amount, the triol (XIV) with m.p. 90-90.5°, which did not give a depression in mixed melting point with the above described specimen.

Hydrolysis of high-melting trans-2-methyl-1-hydroxycyclohexylethylene oxide (m.p. 75°) (XXVI) into triol (XX). One g of the trans-glycidol (XXVI)(m.p. 75°) was hydrolyzed with 40 ml distilled water containing 3 ml of glacial acetic acid, as described above. There was obtained thereby 0.7 g of triol (XX) with m.p. 124-125° (from ether) which did not give a depression in mixed melting point with the specimen described above. There was isolated about 0.2 g of triol (XX), additionally, from the mother liquor; this had m.p. 122-123°.

Hydrolysis of trans-glycidol (XXVI) (m.p. 41°) into triol (XXII). Refluxing 0.3 g of glycidol (XXVI) (m.p. 40-41°) for ten hours with 30 ml of water containing 2 ml of glacial acetic acid, followed by cooling the solution, neutralization with sodium bicarbonate and evaporation in vacuum to dryness, and finally extraction of the residue with ether gave 0.25 g of triol (XXII) in the form of colorless prisms with m.p. 111.5-112° (from ether). On hydrolysis of the liquid mixture of glycidols (XXVI) there was isolated triol (XXVII) with m.p. 111.5-112° (from ether).

Found %: C 62.10, 62.18; H 10.37, 10.38. $C_9H_{18}O_3$. Calculated %: C 62.07; H 10.35.

Mixed melting point with triol (XX), whose m.p. is 125-125.5°, was found to be 109-120°.

Acetate of cis-2-methyl-1-vinyl-1-cyclohexanol (XXVIII). Forty four g of the acetate of cis-acetylenic alcohol (VII) was selectively hydrogenated in an equal volume of methanol over palladium catalysts (0.25 g of 5% $Pd/CaCO_3$). The calculated amount of hydrogen was absorbed in four hours (5.75 liters) and the hydrogenation was terminated. Acetate (VII) hydrogenates noticeably more rapidly than does the acetylenic alcohol (V). There was obtained 41 g of the acetate of cis-2-methyl-1-vinyl-1-cyclohexanol (XXVIII) in the form of a colorless liquid.

B.p. 78-78.5° (6 mm), $n^{20}D$ 1.4611.
Found %: C 72.63, 72.54; H 9.92, 9.90. $C_{11}H_{18}O_2$. Calculated %: C 72.53; H 9.89.

Acetate of trans-2-methyl-1-vinyl-1-cyclohexanol (XXIX). Transacetate (XV) (41.6 g) was selectively hydrogenated in 46 ml of methanol over palladium catalyst as described above. The hydrogenation of the trans-acetate (XV) proceeds more rapidly than does that of the cis-acetate (VII) and was completed in three hours. There was obtained 34 g of the acetate of trans-2-methyl-1-vinyl-1-cyclohexanol (XXIX) in the form of a colorless liquid.

B.p. 75-78° (7 mm), $n^{20}D$ 1.4597.
Found %: C 72.47, 72.36; H 9.74, 9.60. $C_{11}H_{18}O_2$. Calculated %: C 72.53; H 9.89.

Oxidation of cis-2-methyl-1-vinyl-1-cyclohexyl- acetate (XXVIII) with peracetic acid. To the solution of 12.7 g of acetate (XXVIII) (b.p. 79° at 6 mm, $n^{20}D$ 1.4611) in 50 ml of chloroform there was added, at 0°, 10 g of 90% peracetic acid and the mixture was left for one month at room temperature. No elevation of temperature of the mixture was observed. After one month the solution contained about 2 g of peracetic acid (the added excess was 2 g). The solution was neutralized with aqueous sodium bicarbonate and dried with sodium sulfate. After a vacuum distillation there was obtained about 3 g of the initial acetate (XXVIII) with b.p. 82-85° (7 mm) and 6.7 g of a viscous colorless sirup with b.p. 145-146° (3 mm), $n^{17}D$ 1.4862, which crystallized gradually. After several recrystallizations from a mixture of ether with petroleum ether there was isolated 1.7 g of colorless crystals consisting of a mixture of crystals of two different forms: prisms with m.p. 58.5-59.5° (0.9 g) and long needles with m.p. 71-72° (0.75 g). By further recrystallization from petroleum ether the fraction with m.p. 71-72° yielded the acetate of the triol (XXX) in the form of silvery white needles with m.p. 99-100°.

Found %: C 61.04, 61.05; H 9.22, 9.24. $C_{11}H_{20}O_4$. Calculated %: C 61.11; H 9.26.

The acetate of triol (XXXI) was isolated in the form of silvery white needles with m.p. 57-58°, after several recrystallizations of the fraction with m.p. 58.5-59.5° from petroleum ether.

Found %: C 61.22, 61.37; H 9.32, 9.33. $C_{11}H_{20}O_4$. Calculated %: C 61.11; H 9.26.

The mixed melting point with acetate (XXX) (m.p. 99-100°) was 57.5-85°. Acetate (XXXI) is more difficultly soluble in petroleum ether than is acetate (XXX).

Hydrolysis of cis-2-methyl-1-acetoxycyclohexyl glycol (XXX) (m.p. 99-100°) into triol (XII). The solution of 0.15 g of acetate (XXX) (m.p. 99-100°) in 20 ml of ethanol was refluxed for four hours with 10 ml of 0.5 N alcoholic solution of potassium hydroxide. The excess alkali was back titrated on the following day with 0.1 N solution of sulfuric acid. Six and eight tenths ml of 0.1 N solution of potassium hydroxide was consumed in the hydrolysis, which amount corresponded to one acetate group. After neutralization of the solution, followed by evaporation and extraction, with a subsequent crystallization from petroleum ether, there was isolated 0.08 g of triol (XII) with m.p.87-88°, which did not give a mixed melting point depression with a specimen described above. The hydrolysis of acetate (XXX) does not proceed to completion after boiling for one hour.

Hydrolysis of cis-2-methyl-1-acetoxycyclohexyl glycol (m.p. 57-58°) (XXXI) into triol (XIV). Acetate (XXXI) (m.p. 57-58°) (0.36 g) and 10 ml of 0.5 N alcoholic solution of potassium hydroxide were refluxed for one hour. Henceforth the experiment was conducted as described above. The consumption of 0.1 N solution of potassium hydroxide for the hydrolysis was 16.7 ml, which amount corresponded to the presence in it of one acetate group. From the solution there was isolated, by evaporation and extraction with ether, 0.04 g of triol (XIV) with m.p. 90-90.5°, which did not give a depression of mixed melting point with a specimen described above. An additional amount of 0.2 g of crystals with m.p. 71-72° was isolated from the mother liquor.

Oxidation of the acetate of trans-2-methyl-1-vinyl-1-cyclohexanol (XXIX) with peracetic acid. By an oxidation of 12.7 g of acetate (XXIX) (b.p. 75-80° at 7 mm, $n^{20}D$ 1.4595) in 50 ml of chloroform with 10 g of 90% peracetic acid, as described above, there was obtained about 5 g of a mixture of acetates of triol (XXXIV) in the form of a colorless uncrystallizable sirup.

B.p. 148.5-149° (4 mm), $n^{20}D$ 1.4850.

Found %: C 61.27, 61.43; H 9.30, 9.22. $C_{11}H_{20}O_4$. Calculated %: C 61.11; H 9.26.

Hydrolysis of the mixture of trans-2-methyl-1-acetoxycyclohexyl glycols (XXXIV). Preparation of triols (XXII) and (XXVII). A solution of 1.81 g of the above described mixture of acetates (XXXIV) (b.p. 148.5-149° at 4 mm) in 50 ml of 0.5 N alcoholic solution of potassium hydroxide was refluxed for two hours. Eighty four ml of 0.1 N potassium hydroxide solution was consumed in the hydrolysis, which amount corresponded to the presence of one acetate group in acetate (XXXIV). The neutralized solution was worked up as indicated above. Hereby there was obtained 0.7 g of crystals with m.p. 105-108° and 0.7 g of partly crystallizable sirup. By additional crystallizations from a mixture of ether and iso-octane, fraction with m.p. 105-108° gave 0.35 g of triol (XXVII) in the form of colorless plates with m.p. 111.5-112°, which did not give a depression of mixed melting point with the above described specimen. From the mother liquor there was isolated 0.05 g of triol (XXII) in the form of silvery white crystals with m.p.86-87° (from petroleum ether, b.p. 95-110°).

Found %: C 62.24, 62.13; H 10.46, 10.24. $C_9H_{18}O_3$. Calculated %: C 62.07; H 10.35.

A mixed melting point with the sample of triol (XXII), obtained above, (m.p. 88-88.5°) was 87-88°. Mixed melting point with triol (XXVII) (m.p. 111.5-112°) was 86-109° (moistens at 85°). Mixed melting point with triol (XII) (m.p. 88-88.5°) was 55-60°. Mixed melting point with triol (XIV) (m.p. 90-90.5°) was 20° (took place during rubbing of the specimen on glass). Mixed melting point with triol (XX) (m.p. 125-125.5°) was 108-114°.

Hydration of cis-2-methyl-1-ethynyl-1-cyclohexanol (V). A solution of 28 g of cis-acetylenic alcohol (V) (m.p. 56-57°) in 100 ml of methanol was added with stirring over one hour at 18° to an aqueous methanolic solution of 10 g of mercuric sulfate and 25 g of concentrated sulfuric acid (in 100 g of water and 75 ml of methanol). The formation of a white cheesy precipitate was observed. The reaction temperature was maintained at 18-19°. The hydration reaction was controlled by the acetylenic test (formation of silver acetylide with ammoniacal solution of silver nitrate). The acetylenic test was positive after five hours. The reaction mixture was stirred for 6.5 hours at 19°, on the following day, until the acetylenic test became negative. The solution was diluted to twice the volume with water, neutralized with sodium bicarbonate, filtered and evaporated in vacuum. The residue was extracted with ether, dried with sodium sulfate and distilled. There was obtained 25 g of cis-2-methyl-1-acetyl-1-cyclohexanol (XXXV) in the form of colorless viscous liquid.

B.p. 92-93° (8 mm),* m.p. 37-38° (from petroleum ether), $n^{20}D$ 1.4735, $d^{20}_4$ 1.0226, $MR_D$ 42.83; calculated 43.10.

Semicarbazone of (XXXV) formed small colorless crystals with m.p. 228-229° (from ethanol) [4].

Acetate of cis-2-methyl-1-acetyl-1-cyclohexanol (XXXVII). To the solution of 10 g of α-ketol (XXXV) (m.p. 37-38°) in 50 ml of ether there was added 20 g of acetyl chloride and the solution was refluxed for four hours with protection from access of moisture by means of a calcium chloride tube. The yellowish solution was then evaporated in vacuum and the residue was distilled in vacuum. There was obtained 11 g of the acetate of cis-2-methyl-1-acetyl-1-cyclohexanol (XXXVII) in the form of a colorless liquid.

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* Author of [4] mistakenly assigned the lower b.p. (81-82° at 12 mm) to the crystalline isomer.

B.p. 121-122° (12 mm), $n^{20}D$ 1.4629, $d^{20}_4$ 1.0470. $MR_D$ 52.58; calculated 52.46.
Found %: C 66.90, 66.72; H 9.27, 9.15. $C_{11}H_{18}O_3$. Calculated %: C 66.66; H 9.10.

The same result was obtained in acetylation of α-ketol (XXXV) with acetic anhydride in the presence of one drop of sulfuric acid. The acetate (XXXVII) does not form a 2,4-dinitrophenylhydrazone.

Hydration of trans-2-methyl-1-ethynyl-1-cyclohexanol (VI). Trans-acetylenic alcohol (VI) (b.p. 70° at 10 mm, $n^{17}D$ 1.4777) (28 g) was hydrated at room temperature in the presence of mercuric sulfate and concentrated sulfuric acid as described above. The hydration was completed in 5.5 hours (negative test for acetylenic hydrogen with ammoniacal solution of silver nitrate). There was obtained 16 g of trans-2-methyl-1-acetyl-1-cyclohexanol (XXXVI) in the form of a colorless liquid.

B.p. 82-83° (10 mm), $n^{20}D$ 1.4620, $d^{20}_4$ 0.9974. $MR_D$ 43.0; calculated 43.10 [4].
Literature data [4]: b.p. 92° (10 mm),* $n^{20}D$ 1.4635.
Found %: C 68.91, 68.71; H 10.40, 10.36. $C_9H_{16}O_2$. Calculated %: C 69.23; H 10.34.

A somewhat better yield of trans-α-ketol (XXXVI) was obtained in the hydration of acetylenic alcohol (VI) at the temperature of 60-72°.

Semicarbazone of trans-α-ketol (XXXVI) forms colorless crystals with m.p. 217-218° (from ethanol) [4]. Mixed melting point with semicarbazone of cis-α-ketol (XXXV) (m.p. 228-229°) was 200-203°.

The liquid trans-α-ketol (XXXVI) has a lower boiling point, index of refraction and specific gravity than does the crystalline cis-isomer (XXXV). This fact indicates that the Auwers-Skita rule is applicable to 1,2-gem substituted cyclohexanes as well.

Acetate of trans-2-methyl-1-acetyl-1-cyclohexanol (XXXVIII). To 20 g of freshly distilled acetic anhydride containing one drop of concentrated sulfuric acid there was added dropwise 10 g of trans-α-ketol (XXXVI) (b.p. 80-86° at 10 mm, $n^{18}D$ 1.4630). The reaction temperature was kept from rising above 20° by means of water cooling. On the following day the solution was heated for two hours to 50-70°, diluted with four volumes of water, neutralized with sodium bicarbonate, extracted with ether and dried over sodium sulfate. There was obtained 10 g of the acetate of trans-2-methyl-1-acetyl-1-cyclohexanol (XXXVIII) in the form of a colorless liquid.

B.p. 115.5-116.5° (12 mm), $n^{20}D$ 1.4590, $d^{20}_4$ 1.0383. $MR_D$ 52.13; calculated 52.46.
Found %: C 66.22, 66.20; H 8.99, 9.10. $C_{11}H_{18}O_3$. Calculated %: C 66.66; H 9.10.

Acetate (XXXVIII) does not form a 2,4-dinitrophenylhydrazone.

Trans-α-ketol (XXXVI) is not acetylated by acetyl chloride in ether and in pyridine, as well as by refluxing with acetic anhydride without a catalyst.

## SUMMARY

1. The stereochemistry of reactions of introduction of dihydroxycarboxylic, glyceryl and α-ketolic side chains was studiedwith the example of o-methylcyclohexanone.

2. It was shown for the first time that the intramolecular rearrangement of acetates of cis- and trans-2-methyl-1(ω-dibromoacetyl)-1-cyclohexanol does not proceed stereospecifically but forms all four racemic dihydroxy carboxylic acids which are predictable by theory – cis-2-methyl-1-hydroxycyclohexylglycolic acids (erythro-threo isomerism) and trans-2-methyl-1-hydroxycyclohexylglycolic acids (erythro-threo isomerism).

3. The reduction of the indicated dihydroxy acids with lithium aluminum hydride was accomplished, yielding the corresponding triols: cis-2-methyl-1-hydroxycyclohexyl glycols (erythro-threo isomerism) and

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* Evidently the higher boiling point, which pertains to the cis-isomer, was mistakenly assigned to the trans-isomer.

trans-2-methyl-1-hydroxycyclohexyl glycols (erythro-threo isomerism), which were obtained also by the hydrolysis of stereoisomeric glycidic alcohols – cis- and trans-2-methyl-1-hydroxycyclohexylethylene oxide (erythro-threo isomerism).

4. It was shown that in contrast to tertiary vinyl alcohols, the cis- and trans-vinyl-2-methyl-cyclohexanols, the oxidation of the acetates of these alcohols with peracetic acid proceeds anomalously and, instead of the expected glycidols, yields two cis-2-methyl-1-acetoxycyclohexyl glycols and two trans-2-methyl-1-acetoxycyclohexyl glycols.

5. On the basis of the difference in the rate of acetylation of the cis- and the trans-α-ketols a supposition is expressed about the equatorial and axial conformations of the hydroxyl in cis-2-methyl-1-acetyl-1-cyclohexanol and trans-2-methyl-1-acetyl-1-cyclohexanol respectively.

## LITERATURE CITED

[1] I. N. Nazarov and A. A. Akhrem, J. Gen. Chem. 26, 1186 (1956).*

[2] A. E. Favorskii and N. Vittorf, J. Russ. Chem. Soc. 32, 88 (1900); J. Salomon and T. Reichstein, Helv. Chim. Acta 30, 1616 (1947).

[3] I. N. Nazarov et al., J. Gen. Chem. 23, 1900 (1953);* Bull. Acad. Sci. USSR, Ser. Chem. 1956, 960, 1370.*

[4] J. Billimoria, J. Chem. Soc. 1953, 2626.

[5] N. Malas, N. McDonald and D. Black, J. Am. Chem. Soc. 70, 1829 (1948); J. Heilbron, E. Jones, D. Lewis, and B. Weedon, J. Chem. Soc. 1949, 2023.

[6] I. N. Nazarov, A. V. Kamernitskii and A. A. Akrem, J. Gen. Chem. 28, 1458 (1958).*

[7] G. Chiurdoglu, Bull. Soc. Chim. Belg. 47, 241 (1938).

[8] Sh. Wang and M. Hu, J. of the Chinese Ch. Soc. 10, 1 (1943); N. Deno and J. Johnson, J. Org. Chem. 17, 1466 (1952).

[9] D. Barton and R. Cookson, Quarterly Rev. 10, 44 (1956); H. Orloff, Chem. Revs. 54, 347 (1954); I. N. Nazarov and L. D. Bergel'son, Prog. Chem. USSR 26, 3 (1957).

[10] J. Pasqual, J. Sistare and A. Regas, J. Chem. Soc. 1949, 1943.

[11] M. Murat, Ann. Chim. Phys. 16, 116 (1909).

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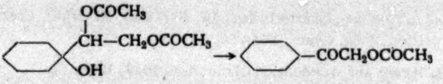
# A STUDY IN THE FIELD OF STEREOCHEMISTRY OF CYCLIC COMPOUNDS

## 28. STERIC DIRECTIVITY OF THE SERINI REACTION IN THE CYCLOHEXANE SERIES

I. N. Nazarov, A. A. Akhrem and A. V. Kamernitskii

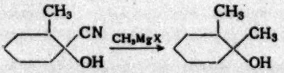
The rearrangement of the secondary monoacetate of secondary-tertiary α-glycols, under the influence of zinc dust, into ketones with the same carbon skeleton, which is known under the name of the Serini reaction, has been studied extensively in the steroid series [1], in which it proceeds strictly stereospecifically and leads to the inversion of configuration at the tertiary carbon atom. The Serini reaction is at present a dependable method of determination of the configuration of the side chain at the 17-carbon atom of steroids.

However to this date there have been no studies devoted to the stereochemistry of the Serini reaction in the series of the simplest cyclic compounds. The only known instance of the transformation of 2,3-diacetate of 1-pentamethyleneglycerol into acetoxymethyl cyclohexyl ketone [2] does not permit one to draw any stereochemical deductions.

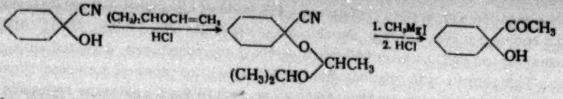


Insofar as it has been established by us [3, 4] the steric structure of isomeric 1-acetyl-2-methylcyclohexanols, which contain two asymmetric centers, appeared to be an example with which one may realize the Serini reaction with interesting results.

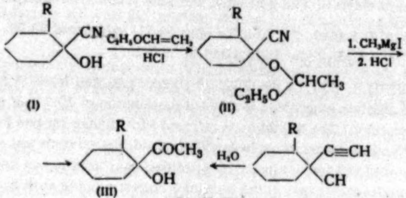
1-Acetyl-2-methylcyclohexanols were prepared both by hydration of 1-ethynyl-2-methylcyclohexanols [4], and by the reaction of cyanohydrins of 2-methylcyclohexanone with methylmagnesium iodide. This permitted us to relate among themselves the stereoisomeric cyanohydrins and acetylenic alcohols derived from 2-methylcyclohexanone, by additional routes. It is known that the direct reaction of cyanohydrins of 2-methylcyclohexanone with methylmagnesium halides leads to decomposition of the cyanohydrins and to formation of the corresponding alcohol [5].



It was shown recently, with the example of cyclohexanone cyanohydrin [6], that a preliminary protection of the hydroxyl group with dihydropyran permits one to conduct a normal reaction with organomagnesium compounds. There is also the communication [7] in which there is indicated the possibility of application, for the hydroxyl protection, of vinyl isopropyl ether.


(CH₃)₂CHOCH=CH₂
HCl
1. CH₃MgI
2. HCl
CN
OH
CN
CHCH₃
(CH₃)₂CHO
COCH₃
OH

We realize the reaction of cyanohydrins of cyclohexanone and cis- and trans-cyanohydrins of 2-methylcyclohexanone with methylmagnesium iodide with the preliminary protection of the hydroxyl group of the cyanohydrins by means of vinyl ethyl ether. The reaction of cyanohydrins (I) with vinyl ethyl ether was run in anhydrous benzene in the presence of an ethereal solution of hydrogen chloride; thereby there were prepared the corresponding acetals (II).

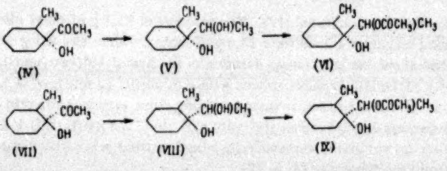

R
CN
OH
C₂H₅OCH=CH₂
HCl
CN
CHCH₃
C₂H₅O
1. CH₃MgI
2. HCl
COCH₃
OH
H₂O
C≡CH
CH

(I) (II) (III)

R = H, CH₃

By the action of methylmagnesium iodide on acetals (II) there were prepared in 75% yield of acetylcyclohexanols (III) which were identical with the ketols formed by hydration of the corresponding acetylenic alcohols.

Stereoisomeric 1-acetyl-2-methylcyclohexanols (IV) and (VII ) were subjected to reduction with aluminum isopropoxide in toluene solution with distillation of acetone. Hereby from cis-ketol (IV) there was obtained only one crystalline 1-(α-hydroxyethyl)-2-methylcyclohexanol (V), which indicates the selectivity of the reduction reaction. The analogous reduction of trans-ketol (VII) led to the isolation of liquid trans-1(α-hydroxyethyl)-2-methylcyclohexanol (VIII).

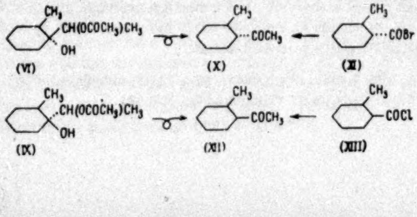

CH₃
COCH₃
OH
CH(OH)CH₃
CH(OCOCH₃)CH₃

(IV) (V) (VI)

(VII) (VIII) (IX)

Glycols (V) and (VIII) gave, after partial acetylation, the corresponding monoacetates (VI) and (IX), among which the first was crystalline, the second – liquid.

In the Serini reaction with acetate (VI) (refluxing with zinc dust in o-xylene for six hours) there was formed trans-1-acetyl-2-methylcyclohexane (X), also prepared from the bromide of trans-hexahydro-o-toluic acid (XI) [3] and methylmagnesium iodide. The mixed melting point of semicarbazones of the two specimens showed no depression.


CH₃
CH(OCOCH₃)CH₃
OH
COCH₃
COBr
COCl

(VI) (X) (XI)

(IX) (XII) (XIII)

The Serini reaction with acetate (IX) gave a 43% yield of cis-1-acetyl-2-methylcyclohexane (XII), also obtained by the convergent synthesis from the chloride of cis-hexahydro-o-toluic acid (XIII) [3]. Besides the indicated ketones (X) and (XII) no other individual carbonyl compounds were detected among the products of the Serini reaction. This permits us to conclude that the Serini reaction proceeds stereospecifically with formation of a configurational inversion at the tertiary carbon atom, both in the cyclohexane series and in the steroid series.

## EXPERIMENTAL

Ethyl-1-cyanocyclohexyl acetal[(II), R=H.] To the solution of 25 g of 1-cyanocyclohexanol [8] and 21.7 g of vinyl ethyl ether in 25 ml of absolute benzene there was added 10 drops of absolute ether saturated with hydrogen chloride. The mixture was cooled and left overnight, after which it was neutralized with solid caustic and distilled in vacuum. There was obtained 33.2 g of ethyl 1-cyanocyclohexyl acetal in the form of a colorless liquid.

B.p. 72-73° (2 mm), $n^{20}D$ 1.4480, $d^{20}_4$ 0.9838. $MR_D$ 53.71; calculated 53.90.
Found %: N 7.72, 7.83. $C_{11}H_{19}O_2N$. Calculated %: N 7.10.

Acetylcyclohexanol[(III),R=H]. To the Grignard reagent prepared from 15.6 g of methyl iodide and 2.7 g of magnesium in 70 ml of absolute ether there was added the solution of 19.7 g of ethyl 1-cyanocyclohexyl acetal in 20 ml of absolute ether. The mixture was refluxed with stirring for one hour; 60 ml of water was added with cooling along with 20 ml of concentrated hydrochloric acid, the mixture was stirred for one hour at 20° and was then neutralized with solid sodium bicarbonate. After the usual working-up and vacuum distillation, there was obtained 11.6 g of acetylcyclohexanol in the form of a colorless liquid with b.p. 58-61° (2.5 mm), $n^{20}D$ 1.4678 [9-12].

The semicarbazone had m.p. 198-199° (from methyl alcohol) and gave no depression in mixed melting point with semicarbazone prepared from the acetylcyclohexanol synthesized by hydration of 1-ethynylcyclohexanol.

Ethyl cis-1-cyano-2-methylcyclohexyl acetal [(II), R=CH$_3$]. From 27.8 g of cis-1-cyano-2-methylcyclohexanol [3] and 21.6 g of vinyl ethyl ether there was obtained, analogously to the above, 33.4 g of ethyl cis-1-cyano-2-methylcyclohexyl acetal in the form of a colorless liquid.

B.p. 80-81° (2.5 mm), $n^{20}D$ 1.4480, $d^{20}_4$ 0.9720. $MR_D$ 58.16; calculated 58.52.
Found %: N 6.62, 6.53. $C_{12}H_{21}O_2N$. Calculated %: N 6.58.

Cis-1-acetyl-2-methylcyclohexanol (IV). The reaction of 21.1 g of ethyl cis-1-cyano-2-methylcyclohexyl acetal with the Grignard reagent obtained from 15.6 g of methyl iodide and 2.7 g of magnesium was run under the conditions described above but with longer duration of the hydrolysis (two hours). After vacuum distillation there was isolated 5.5 g of 2-methylcyclohexanone with b.p. 50-56° (3 mm), $n^{20}D$ 1.4520. Semicarbazone (m.p. 189-191°) did not give a depression in mixed melting point with an authentic sample. There was obtained 8.3 g of cis-1-acetyl-2-methylcyclohexanol (IV) with b.p. 75-77° (3 mm), $n^{20}D$ 1.4720, m.p. 37-38° (from petroleum ether), which did not give a depression in mixed melting point with a specimen prepared by hydration of cis-1-ethynyl-2-methylcyclohexanol [4, 5, 12].

Semicarbazone of the ketol (IV) melted at 229-230° (from alcohol; with decomposition) and similarly did not give a depression in mixed melting point with an authentic sample [4, 5, 12].

Found %: N 19.98, 19.80. $C_{10}H_{19}ON_3$. Calculated %: N 19.71.

Ethyl trans-1-cyano-2-methylcyclohexyl acetal[(II), R=CH$_3$]. To the solution of 27.8 g of liquid mixture of cyanohydrins enriched with trans-1-cyano-2-methylcyclohexanol [3] and 21.6 g of vinyl ethyl ether in 25 ml of anhydrous benzene there was added 10 drops of ethereal solution of hydrogen chloride. The mixture was refluxed for 3.5 hours without access of moisture ; it was then left overnight and then worked up as usual. There was obtained 31.7 g of a mixture of acetals with b.p. 82-89° (3 mm) from which by repeated distillation there was isolated ethyl trans-1-cyano-2-methylcyclohexyl acetal.

B.p. 84.5° (2.5 mm), $n^{20}D$ 1.4490, $d^{20}_4$ 0.9686. $MR_D$ 58.43; calculated 58.52.
Found %: N 6.98, 7.08. $C_{12}H_{21}O_2N$. Calculated %: N 6.68.

Trans-1-acetyl-2-methylcyclohexanol (VII). The above described mixture of acetals (21.1 g) entered into the reaction with the Grignard reagent prepared from 15.6 g of methyl iodide and 2.7 g of magnesium, as described above, with increased duration of hydrolysis to 3.5 hours. After the usual working-up and distillation there was obtained 4.5 g of 2-methyl-cyclohexanone with b.p. 50-55° (3 mm) and 5.9 g of a mixture of stereoisomeric 1-acetyl-2-methylcyclohexanols (IV) and (VII) with b.p. 64-77° (3 mm). By repeated fractional distillation there was isolated the trans-1-acetyl-2-methylcyclohexanol (VII ) with b.p. 58-60° (2.5 mm), $n^{20}D$ 1.4655 [4], the semicarbazone of which melted at 218.5-219° (with decomposition) (from alcohol) and gave no depression in mixed melting point with an authentic sample prepared by hydration of trans-1-ethynyl-2-methylcyclohexanol [4, 5].

Found %: N 20.09, 20.08. $C_{10}H_{19}ON_3$. Calculated %: N 19.71.

When the acetals were introduced into the reaction without a preliminary purification, the yield of the ketols was raised by 5-10%.

Cis-1(α-hydroxyethyl)-2-methylcyclohexanol (V). A mixture of 15.6 g of cis-1-acetyl-2-methylcyclohexanol (IV) (m.p. 37-38°) and 270 g of 38% solution of aluminum isopropoxide in toluene was heated for four hours under a reflux condenser at 210°, after which 50 ml of anhydrous isopropyl alcohol was added and the azeotropic mixture with b.p. 70-80° was distilled until it gave a negative test for acetone. After the addition of 20 ml of additional isopropyl alcohol and refluxing for 1.5 hours, no more acetone was detected in the distillate. The reaction mixture was carefully stirred with 870 ml of 10% sulfuric acid, the toluene layer was separated while the aqueous layer was extracted three times with ether. After drying of the combined extracts with sodium sulfate, evaporation of the solvents and washing the residue with petroleum ether, there was obtained 12 g (76%) of cis-1(α-hydroxyethyl)-2-methylcyclohexanol (V) in the form of colorless needles with m.p. 94-94.5° (from a mixture of ether and petroleum ether).

Found %: C 68.52, 68.58; H 11.55, 11.53. $C_9H_{18}O_2$. Calculated %: C 68.29; H 11.47.

Acetate of cis-1(α-hydroxyethyl)-2-methylcyclohexanol (VI). The solution of 11.4 g of glycol (V) in 15 ml of pyridine and 8 g of acetic anhydride was kept for three days, after which it was acidified with dilute sulfuric acid and thoroughly extracted with ether. The ethereal extract was washed with bicarbonate solution, dried with sodium sulfate and, after the distillation of the solvent, yielded 14.2 g of the acetate of cis-1(α-hydroxyethyl)-2-methylcyclohexanol (XII) in the form of colorless crystals with m.p. 44-45° (from petroleum ether).

Found %: C 65.62, 65.83; H 10.02, 10.00. $C_{11}H_{20}O_3$. Calculated %: C 65.94; H 10.07.

Trans-1(α-hydroxyethyl)-2-methylcyclohexanol (VIII). Trans-1-acetyl-2-methylcyclohexanol (VII) (b.p. 82-83° at 10 mm, $n^{20}D$ 1.4620) (15.6 g) was reduced with 270 g of 38% solution of aluminum isopropoxide in toluene analogously to the above experiment. After distillation of the reaction products there was isolated 3.2 g of the starting ketol (VII) with b.p. 66-68° (4 mm), $n^{20}D$ 1.4610, and 8.2 g (52%) of trans-1(α-hydroxyethyl)-2-methylcyclohexanol (VIII) with b.p. 105° (6 mm), $n^{20}D$ 1.4880.

Found %: C 68.04, 68.07; H 11.38, 11.27. $C_9H_{18}O_2$. Calculated %: C 68.29; H 11.47.

Acetate of trans-1(α-hydroxyethyl)-2-methylcyclohexanol (IX). A solution of 7 g of trans-1(α-hydroxyethyl)-2-methylcyclohexanol (VIII) and 5.1 g of acetic anhydride in 4.4 g of pyridine was kept for two days and after the usual treatment yielded 7.8 g of the acetate of trans-1(α-hydroxyethyl)-2-methylcyclohexanol (IX) with b.p. 104.5° (4.5 mm), $n^{20}D$ 1.4672.

Found %: C 66.41; 66.32; H 9.91, 9.93. $C_{11}H_{20}O_3$. Calculated %: C 65.94; H 10.07.

Trans-1-acetyl-2-methylcyclohexane (X). a) A mixture of 150 g of activated zinc dust and 500 ml of anhydrous o-xylene was heated to boiling with agitation and part of the xylene was distilled off until all moisture had been removed. To the boiling mixture there was added 13 g of the acetate of cis-1(α-hydroxyethyl)-2-methylcyclohexanol (VI) and the mixture was refluxed with stirring for six hours with periodic distillation of acetic acid. The zinc dust was filtered off, washed with ether and the solvents were distilled in vacuum. After distillation of the product in vacuum there was obtained 5 g (52%) of trans-1-acetyl-2-methylcyclohexane (X) in the form of a colorless liquid with b.p. 49.5-51° (5 mm), $n^{20}D$ 1.4565.

The semicarbazone of trans-ketone (X) melted at 175-176° (from aqueous methyl alcohol) and did not give a depression in mixed melting point with an authentic sample. The mixed melting point with the semicarbazone of cis-ketone (XII) was 156-166°.

b) To the solution of 20.5 g of the bromide of trans-hexahydro-o-toluic acid (XI) [3] in 20 ml of absolute ether there was added the Grignard reagent prepared from 2.5 g of magnesium and 14.2 g of methyl iodide in 60 ml of ether, after which the product was hydrolyzed with dilute hydrochloric acid with cooling. By the usual working-up procedure there was isolated 5.6 g of trans-1-acetyl-2-methylcyclohexane (X) with b.p. 58-59° (7 mm), $n^{20}D$ 1.4548. The semicarbazone of the trans-ketone melted at 177-178° and gave no depression in mixed melting point with the above described specimens.

Found %: N 20.98, 21.01. $C_{10}H_{19}ON_3$. Calculated %: N 21.31. According to the literature data [13] the semicarbazone of the trans-ketone (XI) melts at 177-178.5°

Cis-1-acetyl-2-methylcyclohexane (XII). a) The Serini reaction was run as described above with 7 g of acetate (IX) and 100 g of activated zinc dust in 500 ml of absolute o-xylene. There was obtained 2.2 g of cis-1-acetyl-2-methylcyclohexane (XII) with b.p. 58-62° (7 mm), $n^{20}D$ 1.4665. The entire amount of the ketone (XII) was transformed into the semicarbazone which after several recrystallizations from aqueous methyl alcohol had m.p. 182-183° and did not give a depression in mixed melting point with an authentic sample. The mixed melting point with the semicarbazone of trans-ketone (X) (m.p. 177-178°) was 157-163°. After repeated fractional crystallization of the semicarbazone no other individual products could be isolated.

b) The cis-ketone (XII) was synthesized, as described above, from 24 g of the chloride of cis-hexahydro-o-toluic acid (XIII) [3] and the Grignard reagent prepared from 3.6 g of magnesium and 21.3 g of methyl iodide. After distillation there was obtained 9 g of cis-1-acetyl-2-methylcyclohexane (XII) with b.p. 58-62° (7.5 mm), whose semicarbazone melted at 182-183° and did not give a depression in mixed melting point with the preceding specimen.

Found %: N 21.22, 21.02. $C_{10}H_{19}ON_3$. Calculated %: N 21.31.

According to the literature data: semicarbazone of cis-ketone (XII) melts at 182-182.5° [13, 14].

## SUMMARY

It was shown, with the example of stereoisomeric 1-(α-hydroxyethyl)-2-methylcyclohexanols, that the Serini reaction proceeds stereospecifically in the cyclohexane series and leads to inversion of configuration.

The reduction of cis-1-acetyl-2-methylcyclohexanol with aluminum isopropoxide also proceeds stereospecifically, yielding only one of the possible diols: 1-(α-hydroxyethyl)-2-methylcyclohexanol.

## LITERATURE CITED

[1] I. N. Nazarov and L. D. Bergel'son, Chemistry of Steroidal Hormones; Moscow, 1955.*

[2] A. Ia. Berlin and L. V. Sokolova, J. Gen. Chem. 24, 1874 (1954).**

[3] I. N. Nazarov, A. V. Kamernitskii and A. A. Akhrem, J. Gen. Chem. 28, 1458 (1958).**

[4] I. N. Nazarov and A. A. Akhrem, J. Gen. Chem. 28, 1791 (1958).**

[5] J. D. Billimoria, J. Chem. Soc. 1953, 2626.

[6] J. Elphimoff-Felkin, Comptes rend. 236, 387 (1953); Bull. Soc. Chim. 1955, 784.

[7] B. Tchoubar, Comptes rend. 237, 1006 (1953).

[8] I. N. Nazarov, A. A. Akhrem and A. V. Kamernitskii, J. Gen. Chem. 25, 1345 (1955).**

[9] A. E. Favorskii and L. I. Kolotova, J. Russ. Chem. Soc. 44, 1390 (1912).

[10] J. D. Billimoria and N. F. Maclagan, Nature 167, 81 (1951).

[11] G. W. Stacy and C. A. Hainley, J. Am. Chem. Soc. 73, 5911 (1951).

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*In Russian.

**Original Russian pagination. See C. B. Translation.

[12] D. Papa, H. F. Ginsberg and F. J. Villani, J. Am. Chem. Soc. 76, 4441 (1954).

[13] R. B. Turner, J. Am. Chem. Soc. 72, 878 (1950).

[14] W. G. Dauben and E. Hoerger, J. Am. Chem. Soc. 73, 1504 (1951).

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# THE SYNTHESIS OF MERCAPTOAMINO COMPOUNDS

## III. SYNTHESIS OF 3-MERCAPTO-4-AMINO-2-METHYLBUTANE AND 5-AMINO-1-MERCAPTOPENTANE

Iu. V. Markova, L. N. Zenkova and M. N. Shchukina

The discovery of the protective action against radiation of β-mercaptoethylamine [1] stimulated interest in this class of compounds. In recent years there have been many papers in the literature on the investigation of different derivatives of β-mercaptoethylamine, chiefly its different salts, N⁻, S⁻, N and S substituted compounds, compounds with potential mercapto groups, aminoisothiuronium compounds, and others [2].

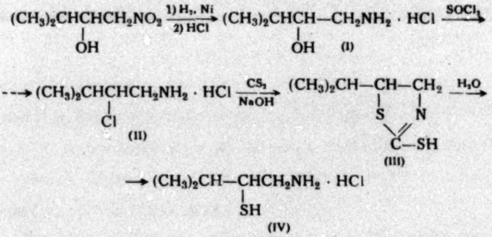
Homologs of β-mercaptoethylamine of the types $R-CH(SH)-CH_2NH_2 \cdot HCl$ and $HS(CH_2)_xNH_2 \cdot HCl$, have been almost unstudied.

It is therefore interesting to study the effect of length and nature of the alkyl chain and also the position of the functional groups by synthesizing a number of compounds of this type.

After we had completed this work, a study was published [3] in which this question received some consideration.

In the present work we have carried out the synthesis of the undescribed 3-mercapto-4-amino-2-methylbutane hydrochloride (IV) (Scheme 1) and 5-amino-1-mercaptopentane hydrochloride (VIII) (Scheme 2).

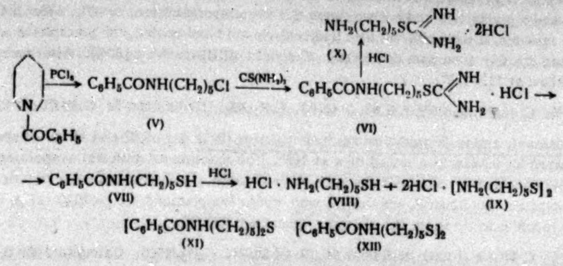
Scheme 1



3-Hydroxy-4-nitro-2-methylbutane, obtained by condensation of isobutyraldehyde with nitromethane [4], was reduced at room temperature in an autoclave in the presence of skeletal nickel to 3-hydroxy-4-amino-2-methylbutane (I), whose hydrochloride was converted to the corresponding chloride (II) by the action of thionyl chloride in dichloroethane. (II) and carbon disulfide gave 2-mercapto-5-isopropylthiazoline (III) which was hydrolyzed by concentrated hydrochloric acid at 160° to 3-mercapto-4-amino-2-methylbutane hydrochloride (IV).

In order to obtain 5-amino-1-mercaptopentane hydrochloride (VIII) from N-benzoylpiperidine, we prepared N-benzoyl-5-amino-1-chloropentane by the method of Braun [5]; the method was modified by simplifying

Scheme 2



the isolation and purification of the preparation and increasing the yield to 63%. (V) was converted by the action of thiourea to N-benzoyl-5-amino-1-isothiuroniumpentane hydrochloride (VI) which was heated with an alkaline solution to give N-benzoyl-5-amino-1-mercaptopentane (VII). (VII) was not formed from (VI) by the action of an alkaline solution at room temperature; it was transformed into the base N-benzoylamino-1-isothiuroniumpentane, from which (VII) could be obtained by further heating with an alkaline solution, or by the action of hydrochloric acid, the starting hydrochloride (VI) could be formed.

Hydrolysis of (VII) was carried out by heating with concentrated hydrochloric acid in a sealed tube at 140-150° for 5 hours, and also by boiling with 20% hydrochloric acid for 20-25 hours. As a result of the hydrolysis we obtained a crystalline substance which contained 70-72% 5-amino-1-mercaptopentane hydrochloride (VIII) and 28-30% of the dihydrochloride of the corresponding oxidized compound bis(5-aminopentyl)disulfide (IX). The presence of the hydrochloride (VIII) was established by iodometric titration, and the presence of the dihydrochloride (IX) was shown by analysis and acetylation of the obtained substance: when it was heated with acetyl chloride, by analogy with the preparation of S-acetylcysteamine hydrochloride [6] and other compounds of this type [7], it gave S-acetyl-5-amino-1-mercaptopentane hydrochloride, and we isolated bis(5-aminopentyl)disulfide dihydrochloride which was present in the starting material as an impurity.

Boiling (VI) with 20% hydrochloric acid for 8 hours gave an almost quantitative yield of 5-amino-1-isothiuronium dihydrochloride (X). When the latter was boiled with an equimolecular amount of alkali for 2 hours, and also when heated in a sealed tube at 140°, it gave a substance whose picrate had a m.p. 138-140° and whose formula was $C_6H_{15}N_3S \cdot C_6H_3O_7N_3$, that is, it corresponded to the starting amine. However, attempts to obtain from the picrate or directly from the reaction product the starting hydrochloride (X) gave no positive results. The structure of the substance was studied. Oxidation of (VII) with an alcoholic solution of iodine gave bis(N-benzoyl-5-aminopentyl) disulfide, and condensation of the same material with (V) in the presence of sodium alcoholate gave bis(N-benzoyl-5-aminopentyl)sulfide.

## EXPERIMENTAL

3-Hydroxy-4-amino-2-methylbutane hydrochloride (I). To a solution of 17 g of 3-hydroxy-4-nitro-2-methylbutane [4] in 85 ml of ethyl alcohol was added 15 g of Raney nickel catalyst (paste) in alcohol. Hydrogenation was carried out at room temperature in an autoclave for 2 hours. After separation of the catalyst, the alcohol solution was acidified with hydrochloric acid and evaporated in a vacuum; the residue was recrystallized from alcohol. The yield was almost quantitative. M.p. 110° (decomp.) The literature [8] gives 110°.

3-Chloro-4-amino-2-methylbutane hydrochloride (II). To a suspension of 14 g of (I) in 100 ml of dry dichloroethane was added 13 g of thionyl chloride with stirring. The reaction mass was boiled 2 hours on the water bath, upon which the substance quickly dissolved, and then precipitated. After cooling, the precipitate was filtered, washed with dichloroethane, and dried in a vacuum desiccator. The yield of (II) was 14.8 g (92%). After recrystallization from alcohol, the substance had a melting point > 190°.

Found %: C 38.18; H 8.28; N 8.75; Cl 45.14. $C_5H_{13}NCl_2$. Calculated %: C 37.98; H 8.29; N 8.86; Cl 44.86.

2-Mercapto-5-isopropylthiazoline (III). To a solution of 5 g of (II) in 15 ml of water was added with stirring 10.5 ml of 24% sodium hydroxide solution and 2.4 g of carbon disulfide. The solution rapidly became yellow, then cloudy, and a precipitate came down; upon this the temperature rose to 40°. After the solution had been stirred for 30 minutes, it was acidified with hydrochloric acid and cooled, the precipitate was filtered off, washed with water, and dried in a vacuum desiccator. The yield of (III) was 3.4 g (80%). After recrystallization from alcohol it melted at 111-112°.

Found %: C 45.29; H 6.85; N 8.66; S 40.23. $C_6H_{11}NS_2$. Calculated %: C 44.70; H 6.87; N 8.73; S 39.70.

3-Mercapto-4-amino-2-methylbutane hydrochloride (IV). 1 g of (III) and 15 ml of concentrated hydrochloric acid were heated for 6 hours in a sealed tube at 160°. The reaction solution was evaporated to dryness in a vacuum; the residue was dissolved in anhydrous alcohol. After addition of anhydrous ether to the alcohol solution to cloudiness, the precipitate was filtered, and washed with ether. We obtained 0.8 g of (IV). M.p. 214-218° (decomp.) According to iodometric titration, the substance contained 95% (IV).

Found %: C 38.43; H 8.91; N 8.48; S 20.19; Cl 22.84. $C_5H_{14}NSCl$. Calculated %: C 38.56; H 9.06; N 8.70; S 20.59; Cl 22.74.

N-Benzoyl-5-amino-1-chloropentane (V). A mixture of 935 g of N-benzoylpiperidine and 105 g of phosphorus pentachloride was carefully heated until reaction began, after which it was boiled 30-40 minutes to the formation of a homogeneous solution. After it had cooled, the reaction solution was poured with stirring over cracked ice; the substance then precipitated in the form of an oil which crystallized with further stirring; it was neutralized by grinding with a cold 40% solution of sodium hydroxide, filtered, and washed with ice water and petroleum ether. The yield of (V) was 70 g (62.6%). After recrystallization from alcohol, it melted at 64-65°. According to the literature [5] the m.p. is 66°.

N-Benzoyl-5-amino-1-isothiuronium pentane hydrochloride (VI). 22.6 g of (V), 7.6 g of thiourea, and 60 ml of anhydrous alcohol were refluxed for 6 hours. The precipitate which separated on cooling was filtered off and washed with alcohol and ether. We obtained 17 g of (VI). M.p. 174-176°. After the mother liquors had been evaporated in a vacuum and cooled they yielded 3 more g of (VI). The total yield was 66.2%. After recrystallization from alcohol the substance melted at 180-181.5°. It was difficultly soluble in cold water and cold alcohol.

Found %: C 51.92; H 6.90; N 13.57; S 10.62; Cl 12.14. $C_{13}H_{20}N_3SCl$. Calculated %: C 51.73; H 6.68; N 13.92; S 10.62; Cl 11.75.

The base of this compound was obtained from (VI) by treatment with alkali at room temperature. The compound crystallized with one molecule of water. M.p. 105-107° (from alcohol).

Found %: N 14.84; S 11.23. $C_{13}H_{19}ON_3S \cdot H_2O$. Calculated %: N 14.82; S 11.31.

N-Benzoyl-5-amino-1-mercaptopentane (VII). To a solution of 20 g of N-benzoyl-5-amino-1-isothiuronium pentane hydrochloride in 300 ml of water was added 22 ml of 12% sodium hydroxide. The reaction mass was boiled for 10 minutes. The substance quickly dissolved, then an oil precipitated, which crystallized on cooling. The precipitate was filtered, washed with water, and dried in a vacuum desiccator. The yield of (VII) was 14 g (95.3%). M.p. 72-75°. After recrystallization from 70% alcohol it melted at 76-77°.

Found %: C 64.66; H 7.52; N 6.23; S 14.70; SH 14.70. $C_{12}H_{17}ONS$. Calculated %: C 64.53; H 7.67; N 6.27; S 14.35; SH 14.80.

Bis(N-benzoyl-5-aminopentyl)disulfide (XII). To a solution of 4 g of (VII) in 50 ml of alcohol was added a 2% alcoholic solution of iodine until a yellow color appeared. The resulting precipitate was filtered and recrystallized from alcohol. The yield of (XII) was 3.5 g (87.5%). M.p. 133-135°. According to the literature [9] it melts at 132-133°.

Bis(N-benzoyl-5-aminopentyl)sulfide (XI). To 0.23 g of metallic sodium in 20 ml of anhydrous alcohol was added with stirring 2.23 g of (VII) and then 2.25 g of (V), after which the reaction mixture was boiled for 1.5 hours. The resulting precipitate was filtered, washed with water, and dried in a vacuum desiccator. The yield was almost quantitative. After recrystallization from alcohol the substance melted at 94-95°. According to the literature [9] the m.p. is 96°.

5-Amino-1-mercaptopentane hydrochloride (VIII) and its disulfide (IX). 5 g of (VII) and 25 ml of concentrated hydrochloric acid were heated in a sealed tube at 140° for 5 hours. The benzoic acid which precipitated was filtered off, and the filtrate, after addition to it of 100 ml of water, was evaporated in a vacuum to dryness. The crystalline residue was dried in a vacuum desiccator over $P_2O_5$. The yield of (VIII) was 3.2 g. M.p. 95-105°. The substance contained 70-72% (VIII). Due to its hygroscopic nature the substance was analyzed without further purification.

Found %: C 38.80; H 8.75; N 6.86. $C_5H_{14}NSCl$. Calculated %: C 38.56; H 9.06; N 9.05.

X-Acetyl-5-amino-1-mercaptopentane hydrochloride. 1 g of (VIII) and (IX) from the previous experiment and 5 ml of acetyl chloride were heated on a water bath at 40° for 30 minutes. At the end of the heating the insoluble precipitate was filtered off and the solution was cooled with ice water. The acetyl derivative which precipitated was filtered, washed with absolute ether, and dried over phosphorus pentoxide in a vacuum desiccator. The yield of acetyl compound was 0.6 g. M.p. 125-130°.

Found %: C 42.33; H 8.23; N 7.70; S 16.60; Cl 17.97. $C_7H_{16}ONSCl$. Calculated %: C 42.52; H 8.15; N 7.79; S 16.21; Cl 17.93.

The insoluble precipitate which was filtered off after heating with acetyl chloride was recrystallized from alcohol with ether. It was compound (IX). A mixed melting point with the same substance obtained by hydrolysis of compound (XII) with hydrochloric acid [9] gave no depression. M.p. 225-235° (decomp). According to the literature [10] the melting point is 230°.

Found %: C 38.80; H 8.42; N 8.55; Cl 22.80. $C_{10}H_{26}N_2S_2Cl_2$. Calculated %: C 38.83; H 8.47; N 9.05; Cl 22.92.

5-Amino-1-isothiuronium pentane dihydrochloride (X). 30.2 g of (VI) and 300 ml of 20% hydrochloric acid were refluxed for 8 hours. The benzoic acid which precipitated on cooling was filtered off, and the filtrate was evaporated to dryness in a vacuum. The residue was dissolved in anhydrous alcohol. After addition of ether the solution gave a precipitate which was filtered and washed with ether. The yield of (X) was 19.8 g (84.6%). M.p. 141-143°.

Found %: C 30.46; H 6.96; N 17.59; S 13.55; Cl 30.44. $C_6H_{17}N_3SCl_2$. Calculated %: C 30.76; H 7.13; N 17.98; S 13.69; Cl 30.28.

## SUMMARY

1. We have carried out the synthesis of 3-mercapto-4-amino-2-methylbutane hydrochloride and 5-amino-1-mercaptopentane and its acetyl derivative.

2. We have shown that in the hydrolysis of N-benzoyl-5-amino-1-mercaptopentane by hydrochloric acid, along with the formation of 5-amino-1-mercaptopentane hydrochloride, there is partial oxidation of the latter to the corresponding disulfide.

3. From N-benzoyl-5-amino-1-isothiuronium pentane dihydrochloride by acid hydrolysis we have obtained 5-amino-1-isothiuronium pentane dihydrochloride which is not hydrolyzed by heating with alkali.

4. In the oxidation of N-benzoyl-5-amino-1-mercaptopentane by alcoholic iodine we have obtained bis(N-benzoyl-5-aminopentyl)-disulfide, and by condensation of the same starting material with N-benzoyl-5-amino-1-chloropentane, bis(N-benzoyl-5-aminopentyl)sulfide.

5. We have worked out a satisfactory process for obtaining N-benzoyl-5-amino-1-chloropentane with a yield of 63%.

## LITERATURE CITED

[1] Z. M. Bacq and A. Herve, Arch. Intern. Physiol. 59, 442 (1951); Z. M. Bacq and A. Herve, Fortschr. Röntgenpraxis, Beiheft 77, 44 (1952); Z. M. Bacq and A. Herve, Schweiz. Med. Wochenschr. 40, 1018 (1952); Z. M. Bacq, G. Dechamps, P. Fischer, A. Herve, H. Le Behan, J. Lacomte, M. Pirotte and P. Rayet, Science 117, 633 (1953).

[2] Z. M. Bacq and P. Alexander, Fundament. of Radiobiol. 1955, 290; Z. M. Bacq, S. F. Cousens, M. Fox and A. Herve, Radiat. res. 2, 4, 392 (1955); D. G. Doherty, and W. T. Burnett, Proc. Soc. exp. biol. med. 89, 312 (1955).

[3] H. Langendorf and R. Koch, Strahlentherapie 99, 567 (1956).

[4] Cf. E. Schmidt, A. Ascheri and L. Mayer, Ber. 58, 2431 (1925).

[5] J. Braun, Ber. 37, 2916 (1929).

[6] Th. Wieland and E. Bokelmann, Lieb. Ann. 576, 20 (1952).

[7] Th. Wieland and H. Horning, Lieb. Ann. 600, 13 (1956).

[8] K. A. Krasusskii and F. F. Krivonos, Ukrain. Khim. Zhur. 4, 82 (1929).

[9] Z. Fõldi, Ber. 62, 1701 (1929).

[10] W. Dirscherl and F. W. Weingarten, Lieb. Ann. 574, 131 (1951).

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# THE REACTION OF DINITRODIOLEFINS WITH COMPOUNDS WHICH CONTAIN MOBILE HYDROGEN IN METHYLENE GROUPS*

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The chemistry of unsaturated nitrocompounds has developed almost entirely in the direction of seeking effective methods of synthesis and studies of the transformations of aliphatic, aromatic, and heterocyclic mononitroolefins. Great progress has been made in this field [1-4].

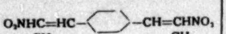
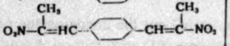
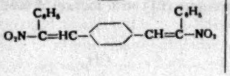
Up to now, compounds which contain two nitro groups have been little studied. It is only known that some of them combine with ammonia, aniline, bromine [5, 6], and mercaptans [7], and after condensation with phenylnitromethane and p-bromophenylnitromethane they are converted into isoxazoline oxides [5]. It has also been shown that dinitrodiolefins obtained by condensation of terephthalic aldehyde with nitromethane have an increased antibacterial activity [8].

In this connection it is important to study methods of synthesis of some dinitrodiolefins, derivatives of terephthalic aldehyde, and their reactions with compounds which contain mobile hydrogen atoms in the methylene group.

When ethylenediamine is used as a catalyst [9] and the usual method of condensation of terephthalic aldehyde with nitromethane is changed [5, 10], it is possible in special cases to increase considerably the yield of dinitrodiolefins (Table 1).

TABLE 1

Obtaining Dinitrodiolefins

| Substance | Dinitrodiolefin | Catalyst | Yield (in %) | Literature data | |
|---|---|---|---|---|---|
| | | | | catalyst | yield (in %) |
| (I) |  $O_2NHC{=}HC{-}C_6H_4{-}CH{=}CHNO_2$ | Sodium hydroxide | 67 | Sodium hydroxide<br>n-Butylamine | * [10]<br>31 [8] |
| (II) |  $O_2N{-}C(CH_3){=}HC{-}C_6H_4{-}CH{=}C(CH_3){-}NO_2$ | Ethylenediamine | 47 | n-Amylamine | 43 [5] |
| (III) |  $O_2N{-}C(C_2H_5){=}HC{-}C_6H_4{-}CH{=}C(C_2H_5){-}NO_2$ | Ethylenediamine | 46 | | |

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* The yield is not given in this work; according to our experiments, it is 5-6%.

The dinitrodiolefins which were obtained were reacted with a series of substances which contained mobile hydrogen atoms in the methylene group: malonic and acetoacetic esters, phenylmethylpyrazolone, cyanoacetic and nitroacetic esters, and phenylnitromethane.

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* Previous communication, see J. Gen. Chem. 28, 675 (1958).

In the nitroolefins which we used, the nitro groups at opposite ends of the molecule caused different behavior in the conjugated systems. This increased the interest in the study, since the question of the reactivity of nitrocompounds with such structures is still open.

First of all, and in greatest detail, we studied 1,4-bis(β-nitrovinyl)benzene (I).

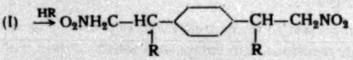
Attempts to combine diethyl malonate with this dinitrodiolefin in the presence of organic bases did not give positive results. However, its reaction with sodium malonic ester in anhydrous ethanol or methanol was carried out successfully with the formation of the ethyl (IV) and methyl esters (V) of the condensation product. In methanol solution under the influence of sodium methylate there first occurred transesterification of diethyl malonate [11], and then reaction of the sodium dimethyl malonate which was formed with the dinitrodiolefin(I); the condensation product in this case did not undergo any transesterification.

Condensation of cyanoacetic ester with the dinitrodiolefin(I) under the catalytic influence of triethylamine [12] proceded very easily even in the cold, but the isolation and purification of reaction product (VI) was very difficult; this difficulty was removed when triethyl amine was replaced by sodium methylate.

Acetoacetic ester in the presence of pyridine, piperidine, and dimethylaniline did not react with dinitrodiolefin(I). The expected condensation product (VII) was obtained in 83% yield after short boiling of the starting substance in methanol solution in the presence of triethylamine.

Under the catalytic influence of triethylamine the dinitrodiolefin(I) reacts very easily with phenylmethylpyrazolone, forming a high yield of product (VIII).

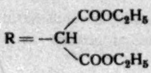
The use of triethylamine also permitted us to carry out the combination with the dinitrodiolefin (I) of nitroacetic ester and phenylnitromethane, as a result of which reactions we synthesized products (IX) and (X).



$$\text{(I)} \xrightarrow{HR} O_2NH_2C{-}\underset{R}{HC}{-}C_6H_4{-}\underset{R}{CH}{-}CH_2NO_2$$

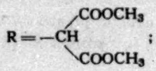
(IV—X)

(IV)



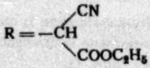
$$R = {-}CH(COOC_2H_5)_2$$

(V)



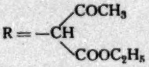
$$R = {-}CH(COOCH_3)_2$$

(VI)



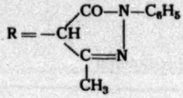
$$R = {-}CH(CN)(COOC_2H_5)$$

(VII)



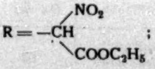
$$R = {-}CH(COCH_3)(COOC_2H_5)$$

(VIII)



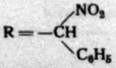
$$R = {-}CH{<}\begin{smallmatrix}CO{-}N{-}C_6H_5\\ C(CH_3){=}N\end{smallmatrix}$$

(IX)



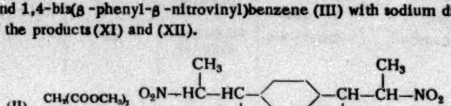
$$R = {-}CH(NO_2)(COOC_2H_5)$$

(X)



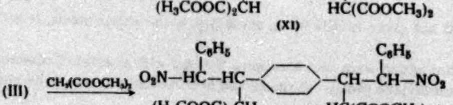
$$R = {-}CH(NO_2)(C_6H_5)$$

To determine the reactivity of other dinitrodiolefins, we carried out the condensation of 1,4-bis(β-methyl-β-nitrovinyl)benzene (II) and 1,4-bis(β-phenyl-β-nitrovinyl)benzene (III) with sodium dimethyl malonate, completing the synthesis of the products (XI) and (XII).



$$\text{(II)} \xrightarrow{CH_2(COOCH_3)_2} O_2N{-}\overset{CH_3}{HC}{-}\underset{(H_3COOC)_2CH}{HC}{-}C_6H_4{-}\underset{HC(COOCH_3)_2}{CH}{-}\overset{CH_3}{CH}{-}NO_2$$

(XI)

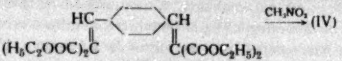


$$\text{(III)} \xrightarrow{CH_2(COOCH_3)_2} O_2N{-}\overset{C_6H_5}{HC}{-}\underset{(H_3COOC)_2CH}{HC}{-}C_6H_4{-}\underset{HC(COOCH_3)_2}{CH}{-}\overset{C_6H_5}{CH}{-}NO_2$$

(XII)

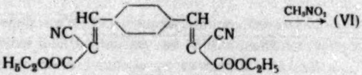
The dinitrodiolefins (I) and (II) easily combine with sodium dimethyl malonate at temperatures to 10°; dinitrodiolefin (III) under these conditions does not react, but at higher temperatures up to 50° it condenses successfully. Evidently among the studied dinitrodiolefins, (III) is the least active, probably for steric reasons caused by the benzene ring at the double bonds.

We devoted much attention to determining the structures of the reaction products from the dinitrodiolefins and the methylene compounds; this problem was solved by different synthesis. Thus, in the reaction of nitromethane with 1,4-bis(β,β-dicarbethoxyvinyl)benzene (XIII), specially obtained for this purpose from condensation of terephthalic aldehyde with malonic ester [13], we obtained a substance identical with (IV).



(XIII)

In a similar way we established the structure of the reaction product from dinitrodiolefin (I) and cyanoacetic ester: 1,4-bis(β-carbethoxy-β-cyanovinyl)benzene (XIV) condensed with nitromethane to form a compound identical with (VI).



(XIV)

When product (VII) was heated with phenylhydrazine in the presence of sodium bisulfite [14] in ethanol solution, we obtained a phenylmethylpyrazolone derivative identical with the reaction product from dinitrodiolefin (I) and phenylmethylpyrazolone (VIII).

Second synthesis confirmed the structure of the condensation products of 1,4-bis(β-nitrovinyl)benzene with malonic, acetoacetic, and cyanoacetic esters, and phenylmethylpyrazolone, and also made it possible to judge the structures of substances synthesized in a similar way: by the reaction of the dinitrodiolefin (I) with nitroacetic ester and phenylnitromethane, and the diolefins (II) and (III) with malonic ester.

It is important to remark that the studied dinitrodiolefins are more stable to polymerization than are the mononitroolefins of the benzene series. This makes it possible to carry out a number of syntheses (reactions with nitro- and cyanoacetic esters) with greater success than in the case of the mononitroolefins.

We should point out that the dinitrodiolefins react with two moles of the methylene component. It follows from this that with two opposite possible directions for the conjugated system, there is nothing to prevent the condensation of these dinitrodiolefins at both double bonds.

## EXPERIMENTAL

1,4-Bis(β-nitrovinyl)benzene (I). In a three-necked flask was placed 10.7 g of terephthalic aldehyde, 60 ml of methanol, and 10 g of nitromethane, and after it was cooled to −5°, a cold solution of 12.8 g of sodium hydroxide in 20 ml of water was added over 10-15 seconds with energetic stirring; the temperature of the reaction mass rose to 40-45°. The thick, snow white suspension was cooled to 5° and kept at this temperature for 10 minutes, then 120 ml of ice water was added. After several minutes an almost colorless solution formed; it was poured with stirring and cooling into 160 ml of 4 N hydrochloric acid. The resulting precipitate of dinitrodiolefin (I) was filtered, washed with water, sucked dry and dissolved in the minimum amount of boiling acetone; hot ethanol was added to cloudiness and the solution left for crystallization. On the next day we obtained 9 g of large golden needles with m.p. 231-232° (decomp). A test sample of (I) with the dinitrodiolefin synthesized according to Thiele [10] (with exact agreement with his yield of 5-6%) gave no depression of melting point. When the solvent was partly distilled from the residue a further 2.8 g of product with m. p. 229-231° (decomp.) was formed. Total yield 11.8 g (67%).

1,4-Bis(β-methyl-β-nitrovinyl)benzene (II). A solution of 1.34 g of terephthalic aldehyde, 4 g of nitroethane, 2 ml of alcohol and 2 drops of ethylenediamine was kept for 23-25 days at 28-30° in a sealed tube with periodic shaking. The light yellow needles of dinitrodiolefin(II) were filtered off, washed with alcohol, then with ether; m.p. 122-123° (from ethanol). Yield 1.17 g (47%).

1,4-Bis(β-phenyl-β-nitrovinyl)benzene (III). A solution of 1.34 g of terephthalic aldehyde, 2.74 g of phenylnitromethane, 3 ml of benzene and a drop of ethylenediamine was heated 16 hours in a thermostat at 60-65°. The resulting light yellow crystalline precipitate of dinitrodiolefin(III) was filtered, and washed with alcohol; m.p. 229° (decomp.) (from acetone). Yield 1.71 g (46%).

1,4-Bis(α-nitromethyl-β,β-dicarbethoxyethyl)benzene (IV). To a suspension of 1.1 g of 1,4-bis(β-nitrovinyl)benzene in 5 ml of anhydrous ethanol, cooled to −2°, was added over several minutes with good stirring sodium malonic ester prepared by dissolving 0.23 g of metallic sodium in a mixture of 1.8 g of diethyl malonate and 5 ml of anhydrous ethanol. The reaction mass was stirred for 1.5 hours at 2° and then the thick suspension was gradually treated with 20 ml of ethanol and 0.9 g of glacial acetic acid and the colorless precipitate was filtered. Yield 1.95 g (72%).

Colorless crystals with m.p. 158-160° (from a mixture of ethanol and acetone); the product was easily soluble in acetone, not soluble in water or ethanol.

Found %: C 52.88, 52.84; H 6.10, 6.07; N 5.07, 5.14. $C_{24}H_{32}O_{12}N_2$. Calculated %: C 53.33; H 5.96; N 5.18.

1,4-Bis(α-nitromethyl-β,β-dicarbomethoxyethyl)benzene (V). To a suspension of 2.2 g of 1,4-bis(β-nitrovinyl)benzene in 20 ml of anhydrous methanol at 0-5° was gradually added sodium malonic ester, prepared from a solution of 0.46 g of metallic sodium in a mixture of 4 g of diethyl malonate and 5 ml of anhydrous methanol. After 1.5 hours stirring at 0°, 1.5 ml of glacial acetic acid was added by drops to the clear solution; the colorless precipitate was stirred for 1 hour, then filtered and washed with ethanol. Yield 3.7 g (72%). M.p. 161-163° (repeatedly crystallized from a mixture of benzene and acetone). The product was easily soluble in benzene and acetone, not soluble in methanol and ethanol.

Found %: C 49.60, 49.75; H 5.12, 5.60; N 5.96, 6.14. $C_{20}H_{24}O_{12}N_2$. Calculated %: C 49.58; H 4.99; N 5.78.

1,4-Bis(α-nitromethyl-β-carbethoxy-β-cyanoethyl)benzene (VI). To a suspension of 1.1 g of 1,4-bis(β-nitrovinyl)benzene, and 1.15 g of ethyl cyanoacetate in 10 ml of anhydrous methanol, cooled to −5°, was added over 5 minutes at a temperature not above 0°, a solution of sodium methylate prepared by dissolving 0.23 g of metallic sodium in 7 ml of anhydrous methanol.

The reaction mass was stirred for 20-30 minutes with cooling, and the resulting clear solution was treated with 0.8 ml of glacial acetic acid, added by drops over 0.5 hour. For full separation of the condensation product, the reaction mass was kept for 4-6 hours at 0-5° in a refrigerator. The heavy precipitate was filtered and washed with methanol.

Colorless crystals with m.p. 170-171° (from acetone with later addition of methanol); soluble in acetone and ethyl acetate, not soluble in benzene and chloroform. Yield 1.7 g (76%).

Found %: N 12.59, 12.46. $C_{20}H_{22}O_8N_4$. Calculated %: N 12.55.

1,4-Bis(α-nitromethyl-β-acetyl-β-carbethoxyethyl)benzene (VII). A mixture of 0.44 g of 1,4-bis(β-nitrovinyl)benzene, 0.65 g of acetoacetic ester, 5 ml of methanol and 2 drops of triethylamine was boiled 20 minutes on the water bath, then heating was stopped and after 3 hours the snow white precipitate was filtered off. M.p. 185-186° (boiled in ethanol), not soluble in water and alcohol, soluble in heated dioxane, acetone, benzene. Yield 0.8 g (86%).

Found %: N 5.85, 5.88. $C_{22}H_{28}O_{10}N_2$. Calculated %: N 5.83.

1,4-Bis[α-4-(1-phenyl-3-methylpyrazolonyl)-β-nitroethyl] benzene (VIII). A mixture of 0.5 g of 1,4-bis(β-nitrovinyl)benzene and 0.9 g of 1-phenyl-3-methyl-5-pyrazolone in 50 ml of methanol was boiled for several minutes on the water bath until solution resulted. Then heating was stopped and 2 drops of triethylamine were added to the reaction mass. After 30 minutes, the slightly colored precipitate of the condensation product was filtered from the still warm solution. Washing the precipitate with hot methanol gave a product with m.p. 246-247° (decomp). Yield 1.1 g (85%).

The slightly colored crystalline product with m.p. 246-247° (from warmed methanol) dissolved easily in mineral acids and alkalis and pyridine, and with more difficulty in boiling glacial acetic acid; it was not soluble in the usual organic solvents.

Found %: C 63.37, 63.33; H 5.44, 5.55. $C_{30}H_{28}O_6N_6$. Calculated %: C 63.37; H 4.96.

1,4-Bis(α-nitromethyl-β-nitro-β-carbethoxyethyl)benzene (IX). A mixture of 0.44 g 1,4-bis(β-nitrovinyl) benzene and 0.72 g of nitroacetic ester in 5 ml of acetone was heated for several minutes on the water bath. After addition of one drop of triethylamine to the suspension, cooled to 50°, a red solution slowly formed and was stirred for an hour more while it cooled by itself. The oily residue after evaporation of the acetone was mixed with 8-10 ml of methanol. The precipitate which separated after several hours was mixed with ether, filtered, and washed with methanol and then ether.

Colorless, transparent needles with m.p. 171-173° (repeatedly crystallized from a mixture of acetone and ethanol); easily soluble in benzene and acetone, insoluble in ethanol and water. Yield 1 g (quantitative).

Found %: C 44.54, 44.79; H 4.85, 5.05; N 11.58, 11.67. $C_{18}H_{22}O_{12}N_4$. Calculated %: C 44.55; H 4.56; N 11.52.

1,4-Bis(α-nitromethyl-β-nitro-β-phenylethyl)benzene (X). To a suspension of 1.1 g of 1,4-bis(β-nitrovinyl)-benzene in a mixture of 1.37 g of phenylnitromethane and 10 ml of methanol at 50-60° was added 2 drops of triethylamine; a heavy, colorless precipitate slowly formed. The reaction mass was boiled for 5 minutes to complete the reaction, then it was cooled and the condensation product was filtered and washed with methanol.

Fine colorless needles with m.p. 219-222° (decomp.) (from acetone with later addition of ethanol); easily soluble in acetone, dioxane, and pyridine; insoluble in methanol, ethanol, benzene, chloroform, and xylene. Yield 2.1 g (85%).

Found %: C 58.21, 58.15; H 4.41, 4.63; N 11.25, 11.69. $C_{24}H_{22}O_8N_4$. Calculated %: C 58.30; H 4.48; N 11.33.

1,4-Bis(α,α-dicarbomethoxymethyl-β-nitropropyl)benzene (XI). To a suspension of 1.24 g of 1,4-bis (β-methyl-β-nitrovinyl)benzene in 7 ml of anhydrous methanol cooled to 0° was gradually added at temperatures not exceeding 5° a solution of sodium malonic ester prepared by dissolving 0.23 g of metallic sodium in a mixture of 2 g of diethyl malonate and 8 ml of anhydrous methanol. Soon after the addition of malonate a clear solution formed, and from it with stirring at 8-10° there gradually formed a heavy precipitate of the sodium salt of the condensation product; after 30 minutes the reaction mass was dissolved by addition of 15 ml of water; 0.1 g of active charcoal was stirred in for 15 minutes at 10-15° and was then filtered off. The colorless filtrate was cooled to 5° and gradually acidified with 1 ml of glacial acetic acid. After 1 hour the snow white precipitate of the condensation product was filtered off and washed with a small amount of methanol and then with water. Fine colorless needles with m.p. 182-183° (from aqueous methanol); easily soluble in the cold in acetone, glacial acetic acid, and hot methanol. Yield 2.35 g (91%).

Found %: C 51.84, 51.58; H 5.73, 5.71; N 5.52, 5.24. $C_{22}H_{28}O_{12}N_2$. Calculated %: C 51.56; H 5.50; N 5.47.

1,4-Bis(α,α-dicarbomethoxymethyl-β-nitro-β-phenylethyl)benzene (XII). To a suspension of 1.11 g of 1,4-bis(β-nitro-β-phenylvinyl)benzene in 5 ml of anhydrous methanol at 15-20° was added a solution of sodium malonic ester, prepared by dissolving 0.14 g of metallic sodium in a mixture of 1.0 g of diethyl malonate and 5 ml of anhydrous methanol. The reaction mass was heated for 30 minutes with stirring to 50° and kept at this temperature for 1 hour. Complete solution of the starting dinitrodiolefin indicated the end of the reaction. The clear solution was cooled to room temperature and acidified with 0.5 g of glacial acetic acid. On the next day the precipitate of the condensation product was filtered and washed with methanol. Yield 1.4 g (73%). Colorless crystalline product with m.p. 193-196° (from a mixture of benzene and methanol); easily soluble in benzene, chloroform, and dichloroethane; more difficultly in acetone, insoluble in methanol.

Found %: C 60.42, 60.30; H 5.29, 5.54; N 4.39, 4.41. $C_{32}H_{32}O_{12}N_2$. Calculated %: C 60.37; H 5.06; N 4.40.

**1,4-Bis(β,β-dicarbethoxyvinyl)benzene (XIII).** A mixture of 2 g of terephthalic aldehyde and 6.4 g of diethyl malonate was heated 20 hours on the boiling water bath in a flask fitted with a reflux condenser and a calcium chloride tube. Each hour after beginning the heating 1 drop of piperidine was added; then the reaction mass was diluted with 20-25 ml of ethanol and the mixture boiled until the precipitate dissolved. The hot solution was filtered from the slight amount of insoluble precipitate and allowed to stand for crystallization. Yield 4.5 g (72%). The colorless crystalline product with m.p. 136-137° (from ethanol) was easily soluble in acetone, hot methanol, and ethanol.

Found %: C 63.25, 63.10; H 6.48, 6.23. $C_{22}H_{26}O_8$. Calculated %: C 63.14; H 6.26.

**1,4-Bis(α-nitromethyl-β,β-dicarbethoxyethyl)benzene (IV).** To a solution of sodium methylate, prepared by dissolving 0.14 g of metallic sodium in 10 ml of anhydrous methanol 0-5°, was added 1.8 g of nitromethane, then 1.26 g of 1,4-bis(β,β-dicarbethoxyvinyl)benzene. The suspension was stirred for 2 hours with the temperature constantly rising to a final value of 25°, at which time a clear solution of the sodium salt of the condensation product had formed. The solution was cooled to 10° and 0.6 g of glacial acetic acid was slowly added. After 30 minutes the resulting precipitate was filtered and washed with methanol. The product had a m.p. of 158-159° (from a mixture of ethanol and acetone); a mixed m.p. with a sample of (IV) gave no depression. Yield 0.7 g (42%).

**1,4-Bis(β-carbethoxy-β-cyanovinyl)benzene (XIV).** To a mixture of 1.34 g (0.01 g-mole) of terephthalic aldehyde, 2.3 g of ethyl cyanoacetate and 40 ml of ethanol was added 1 drop of piperidine with stirring at 20-25°. A clear solution slowly formed, and from it a crystalline condensation product gradually precipitated; it was filtered after 10 hours and washed with methanol. Yield 3.14 g (96%). Yellow-green needles with m.p. 198-199° (from toluene); soluble in hot benzene, acetone, and insoluble in ethanol.

Found %: C 66.58, 66.28; H 5.30, 5.51. $C_{18}H_{16}O_4N_2$. Calculated %: C 66.66; H 4.97.

**1,4-Bis(α-nitromethyl-β-carbethoxy-β-cyanoethyl)benzene (VI).** To a solution of sodium methylate, prepared by dissolving 0.23 g of metallic sodium in 20 ml of anhydrous methanol at 0°, was added 1.5 ml of nitromethane, then in one lot 1.62 g of 1,4-bis(β-carbethoxy-β-cyanovinyl)benzene (XIV). The suspension was stirred 1 hour at 0-2° until a solution was formed, and this was treated at the same temperature over 0.5 hour with 1 ml of glacial acetic acid. At the end of the addition of acid, precipitation began and the colorless precipitate of the condensation product was stirred for 1 hour with cooling, filtered, and washed with methanol. Yield 1.85 g (83%). M.p. 170-171° (twice crystallized from acetone with later addition of methanol). A mixed m.p. with the product (VI) gave no depression.

**1,4-Bis[α-4-(1-phenyl-3-methylpyrazolonyl)-β-nitroethyl]benzene (VIII).** A mixture of 1.2 g of 1,4-bis-(α-nitromethyl-β-acetyl-β-carbethoxyethyl)benzene (VII), 0.54 g of phenylhydrazine and 3 drops of a solution of sodium bisulfite in 10 ml of ethanol was boiled for 1 hour. After the solution had cooled, the precipitate was filtered and washed with ethanol. The product had a m.p. of 250° (decomp.) (from glacial acetic acid). A mixed m.p. with (VIII) gave no depression.

## SUMMARY

1. We have shown that aromatic dinitrodiolefins in the presence of basic catalysts condense with substances which contain a mobile hydrogen atom in the methylene group.

2. We have shown that the presence in the dinitrodiolefins of two oppositely directed conjugated systems does not hinder the condensation process with active methylene components when two nitrovinyl groups take part.

3. The lowest activity of the 1,4-bis(β-phenyl-β-nitrovinyl)benzene among the three nitroolefins which we studied is evidently connected with steric hindrance by the phenyl nucleus on the double bonds.

## LITERATURE CITED

[1] V. V. Perekalin and A. S. Sopova, Usp. Khim. 24, 613 (1955).

[2] V. V. Perekalin and A. S. Sopova, Zh. O. Kh. 28, 675 (1958).*

[3] W. Emerson, Chem. Revs. 45, 183 (1949).

---

*Original Russian pagination. See C. B. Translation.

[4] W. Emerson, Chem. Revs. 45, 347 (1949).

[5] D. Worrall, J. Am. Chem. Soc. 62, 3253 (1940).

[6] P. Ruggli, and O. Schetty, Helv. Chim. Acta, 23, 718 (1940).

[7] A. Mustafa, et. al., J. Am. Chem. Soc. 77, 3860 (1955).

[8] O. Schales and H. Graefe, J. Am. Chem. Soc. 74, 4486 (1952).

[9] O. M. Lerner, Zh. P. Kh. 61, 363 (1958).*

[10] J. Thiele, Ber. 32, 1293 (1899).

[11] M. Reimer, J. Am. Chem. Soc. 43, 950 (1921).

[12] V. V. Perekalin and A. S. Sopova, Zh. O. Kh. 24, 513 (1954).*

[13] E. Kohler and H. Engelbrecht, J. Am. Chem. Soc. 41, 764 (1919).

[14] L. B. Gurvich and O. M. Lerner, Sov. Authors Certificate No. 102089, December 16, 1955.**

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*Original Russian pagination. See C. B. Translation.

**In Russian.

# A STUDY OF IONO-CATALYTIC TELOMERIZATION

## I. TELOMERIZATION OF ISOPRENE WITH ITS HYDROCHLORIDE

K. V. Leets

It was first reported in a patent [1] that it was possible to combine an alkyl halide with a diene hydrocarbon in the presence of ionic catalysts, zinc or tin halides.

Later [2-4] it was shown that this reaction has the character of a telomerization and the formation of one or another reaction product depends on the nature of the starting substance.

With isoprene as an example [3, 5] it was established that the first product of combination of an alkyl halide with isoprene could be obtained in considerable yield only if the telomerization reaction is cut short, stopping the action of the catalyst before 50% of the halogen compound has reacted. These conditions permit the use of the telomerization reaction for carrying out a very simple synthesis of citral from isoprene [6]. In recent work it has been shown that in the telomerization of isoprene with its hydrochloride a mixture of geranyl chloride, isomeric monoterpene chlorides (chiefly terpenyl chloride) and polyterpene chlorides is formed.

In the present paper we give experimental data and theoretical ideas of the author, which prove the importance of the moment of stopping the reaction as one of the main factors which affects the composition of the telomerization products of halogen compounds with dienes.

In this work we have studied the change in composition of the products of telomerization of isoprene with its hydrochloride depending on the intensity of the reaction.*

For the study we used a mixture of isoprene with its hydrochloride obtained by treating isoprene with gaseous hydrogen chloride. [7]. Methylene chloride was the solvent and anhydrous tin chloride was the catalyst. The degree of transformation could be determined by its dependence on the specific gravity of the reaction mixture. The reaction was stopped by removing the catalyst from the reaction mixture with water. The telomer which was obtained was distilled in a vacuum into fractions of monoterpene and polyterpene chlorides, and geranyl chloride was determined in the terpene chlorides by combining it with urotropine [6].

In Figure 1 we give the relation of composition of telomerization products to intensity of reaction, in Fig. 2, the relation of yield of geranyl chloride to the same factor.

As Fig. 1 shows, in the initial stages of the telomerization reaction, the content of all the transformation products in the mixture increases simultaneously, and then begins a rapid growth in content of polyterpene ch-chlorides and a cessation of growth of geranyl chloride. In the final stages of the process the geranyl chloride content falls, at the end of the reaction almost reaching zero. The increase in monoterpene chlorides (terpenyl chloride) is almost constant and only falls at the end of the reaction.

Figure 2 shows that the yield of geranyl chloride is inversely proportional to the intensity of the reaction. Thus, to get a higher yield of geranyl chloride it is necessary to break off the reaction of telomerization at a low intensity.

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* By intensity of the reaction we mean the degree of use of bound and free isoprene, or, in other words, the degree of transformation of isoprene and the hydrochloride into the telomer.

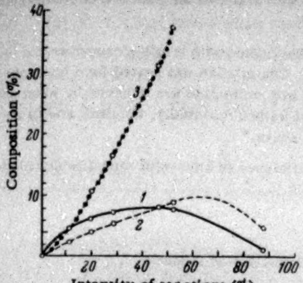

Fig. 1. Composition of telomerization products depending on intensity of reaction. 1) Geranyl chloride; 2) isomeric terpene chlorides; 3) polyterpene chlorides.

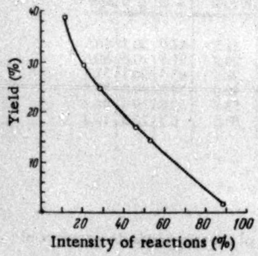

Fig. 2. Yield of geranyl chloride from isoprene (free and bound) which enters the reaction.

This effect can easily be explained on the basis of the earlier ideas [3, 4] of the existence of two kinetic stages in the reaction of combination of halogen derivatives and diene hydrocarbons under the influence of ionic catalysts. As we have shown, the yield of primary combination product depends on the ratio of reactivities of the initial and formed halogen compounds; the primary product can be separated only if the rate of the further reaction with the diene hydrocarbon is less than the rate of its formation. In the case studied, judging by the structure and the mobility of the halogen atom, the corresponding reactivity of the isoprene hydrochloride and the geranyl chloride should be close together. From this it follows that the geranyl chloride obtained from isoprene hydrochloride can react with isoprene to form polyterpene chlorides. The accumulation of geranyl chloride in the mixture in the initial stages of reaction depends on a high concentration of starting isoprene hydrochloride and a small concentration of geranyl chloride, so that the rate of formation of geranyl chloride is much higher than the rate of its destruction. As the starting hydrochloride is used up and the geranyl chloride is formed, the rate of the primary reaction gradually lessens, and that of the second rises. This leads at a certain moment to a kinetic equilibrium between both reactions and the increase of geranyl chloride stops. When the starting halogen is further used up, the second reaction begins to predominate, the content of geranyl chloride in the mixture decreases and in time disappears entirely. Along with this, the content of isomeric monoterpene chlorides in the mixture constantly increases. This is evidently due to their relatively lower reactivity compared to that of the starting halogen compounds, so that they accumulate in the reaction mixture.

## EXPERIMENTAL

Method of conducting the experiments. A round bottomed flask was fitted with a stirrer, reflux condenser, thermometer, and dropping funnel. A glass tube was led to the bottom of the flask and was connected to a small cylindrical vessel with an aerometer. In the flask was placed an equimolecular mixture of isoprene with its hydrochloride and methylene chloride. It was cooled externally with ice and salt and a 2% solution of anhydrous tin chloride in methylene chloride was added with stirring through the dropping funnel until definite signs of reaction appeared (rise of temperature in the mixture). Then the mixture was sucked over into the cylinder with the aerometer with a plastic bulb, and its density was determined at the beginning of the reaction and the mixture was at once forced back into the reaction vessel with the same bulb. Density determinations were carried out every 2 minutes. When the desired density of the reaction mixture had been reached, reaction was stopped by adding a water solution of sodium chloride to the mixture. The product was repeatedly washed with water and dried over potash. The solvent and the unreacted starting reagents were distilled off on the water bath, at first at atmospheric pressure, then in a vacuum. The terpene chloride ($C_{10}$) fraction was distilled from the remaining telomerization product on the water bath at 2-1 mm pressure (b.p. 60-90° at 2 mm).

The geranyl chloride content in a mixture was found in the following way: the total amount of saponifiable chloride in the mixture of chlorides was determined by boiling a sample with an alcohol-water solution of $Pb(NO_3)_2$ for 2 hours. The corresponding amount of acid was then evolved according to the equation.

$$2RCl + Pb(NO_3)_2 + 2H_2O \rightarrow 2ROH + PbCl_2 + 2HNO_3,$$

and after addition of excess aqueous solution of NaCl this was titrated with alkali in the presence of bromphenol blue.

Another sample of chlorides (25 g) was transferred to a 200 ml flask fitted with a reflux condenser and to it was added 20 g of urotropine and 100 ml of dried methylene chloride. The mixture was heated for 3 hours on the water bath. The resulting complex compound of geranyl chloride with urotropine was removed by water and the remaining solution of terpene chlorides in methylene chlorides was washed repeatedly, weighed, and its content of saponifiable chloride was determined by the method described above.*

The geranyl chloride content of the mixture was found by the difference in amount of saponifiable chloride in the starting mixture and in the remaining chlorides.

The results of the experiments are given in tha Table.

Effect of Intensity of Reaction on Composition of the Telomerization Products

| Experiment No. | Composition of reaction mixture (in g) | | | Reaction temperature | Duration of reaction (in min) | Change in mixt. density $d_4^{20}$ | | Telomerization product | | Amt. of isoprene (bound and free) which reacts (in %) | Terpene chloride fraction | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Hydrochloride & isoprene mixt. (20.5% Cl) | solvent | catalyst | | | at beginning of reaction | at end of reaction | yield (in g) | chlorine content (in %) | | yield of telomer (%) | chlorine content (%) | geranyl chloride content (%) |
| 1 | 1430 | 1580 | 0.6 | 18° | 19 | 1.015 | 1.030 | 157 | 17.2 | 11.5 | 64.0 | 20.2 | 63.5 |
| 2 | 1420 | 1600 | 0.6 | 19 | 18 | 1.016 | 1.036 | 272 | 16.4 | 20.2 | 51.5 | 20.0 | 60.6 |
| 3 | 1413 | 1775 | 0.6 | 18 | 31 | 1.043 | 1.069 | 379 | 15.7 | 28.5 | 45.9 | 20.1 | 57.5 |
| 4 | 500 | 770 | 0.4 | 15 | 18 | 1.072 | 1.108 | 212 | 14.9 | 46.6 | 37.2 | 19.6 | 49.8 |
| 5 | 500 | 640 | 0.45 | 20 | 17 | 1.048 | 1.090 | 247 | 14.4 | 53.2 | 33.0 | 19.4 | 46.3 |
| 6 | 300 | 380 | 0.3 | 19 | 68 | 1.046 | 1.148 | 570 | 16.5 | 88.0 | 6.2 | 16.0 | 16.2 |

## SUMMARY

1. We have studied the effect of intensity of reaction on composition of the telomerization product of isoprene and its hydrochloride in the presence of anhydrous tin chloride.

2. We have shown that the intensity of reaction is a decisive factor which determines the composition of the reaction products: in the initial stages of reaction, geranyl chloride predominates in the reaction product, and in the final stages polyterpene chlorides and isomeric monoterpene chlorides (terpenyl chloride) are the main products.

3. We have confirmed the idea which was suggested earlier that it is necessary to interrupt their reaction in the early stages in order to obtain a maximum yield of terpene chlorides in the telomerization of isoprene with halogen compounds.

4. The results of this study have been considered from the viewpoint of the ideas expressed earlier of the two kinetic steps in the process of telomerization in the presence of ionic catalysts.

## LITERATURE CITED

[1] French patent 824909 (1937).

[2] A. A. Petrov and K. V. Leets, DAN SSSR 95, 285 (1954).

[3] K. V. Leets, Dissertation "Study of the Combination of Alkyl Halides with Compounds Which Contain a System of Multiple Bonds," Lensovet Leningrad Tech. Inst. (1954). **

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* Methylene chloride is not saponified in this case.

** In Russian.

[4] A. A. Petrov and K. V. Leets, Zh. O. Kh. 26, 1113 (1956).*

[5] K. V. Leets, Sov. Authors Certificate 105428 (1955).**

[6] K. V. Leets, A. K. Shumeiko and others, Zh. O. Kh. 27, 1510 (1957);* Masloboino-zhirovaia Prom. 23, No. 8, 33 (1957).

[7] A. Ultée, J. Chem. Soc. 1948, 530.

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*Original Russian pagination. See C. B. Translation

**In Russian.

# THE CHLORINATION OF ETHYLENE GLYCOL

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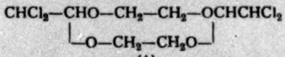
The chlorination of monoatomic alcohols has been studied in sufficient detail. However, there is very little data in the literature on the reaction of chlorine with diatomic alcohols, especially with ethylene glycol. Even in 1863, Mitscherlich [1] noticed an intense reaction of chlorine with ethylene glycol and isolated a fraction with boiled at 108-200° and contained chlorine and a fraction which boiled above 200° and did not contain chlorine. However, the composition of these fractions remained unknown. Later Donciu [2] chlorinated ethylene glycol at 140-180° and obtained a mixture from which he isolated and identified ethylene chlorohydrin, 2-($\beta$-chloroethoxy)-3-hydroxy-1,4-dioxane, and some carbonyl compounds. He also suggested the possibility of forming polyethylene glycol. There are no later studies in the literature.

It appeared interesting to us to investigate this reaction in more detail. Chlorination of ethylene glycol at room temperature without illumination goes very slowly, and so we turned to initiation by ultraviolet light. We then found a very energetic absorption of chlorine by ethylene glycol with evolution of heat so that the temperature of the mixture reached a maximum of 127°. The original weight was increased by 70-80%. As a result we obtained a mixture of products consisting of 27% $\beta$-chloroethyl dichloroacetate, 15% of the previously undescribed cyclic acetal A, 12% water, 11% dichloroacetaldehyde, 11% ethylene chlorohydrin, 6% 2-dichloromethyl-1,3-dioxolane, and small admixtures of oxalic and dichloroacetic acids.



$$\begin{array}{l} CHCl_2-CHO-CH_2-CH_2-OCHCHCl_2 \\ \quad \llcorner O-CH_2-CH_2O \lrcorner \end{array}$$

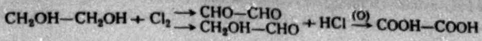
(A)

The structure of the above mentioned acetal was confirmed by splitting it with concentrated hydrochloric acid, as a result of which we obtained dichloroacetaldehyde and ethylene chlorohydrin. The chlorination of ethylene glycol, initiated by the addition of 0.2% $SbCl_5$ gives about the same composition of the mixture as does chlorination in ultraviolet. However, in this case the above mentioned high boiling acetal of ethylene glycol and $CHCl_2CHO$ are absent from the reaction product.

The separation of the different products from the mixture was made difficult by the presence of a large amount of HCl which caused considerable tarring of the products in distillation. Therefore, before separation of the mixture it was carefully freed from HCl.

Since the chief reaction product of chlorination of ethylene glycol in ultraviolet is $\beta$-chloroethyl dichloroacetate, it became interesting to study the action of chlorine on this ester in order to explain the nature of the high boiling products. We ran experiments on the chlorination of this ester in the ultraviolet which showed that we obtained a yield of 62% of $\alpha,\beta,\beta',\beta''$-tetrachloroethyl trichloroacetate.

Thus, in the reaction of chlorine with ethylene glycol under ultraviolet illumination or in the presence of a catalyst the processes of oxidation and chlorination occur simultaneously, accompanied by secondary reactions: esterification and acetal formation. We must assume that here, as in the case of monoatomic alcohols, the first action of chlorine on ethylene glycol is the oxidation of one or two of the hydroxyls with formation of the corresponding glyoxal and glycolic aldehyde, which, however, could not be isolated, evidently because of its rapid transformation to oxalic acid.



$$CH_2OH{-}CH_2OH + Cl_2 \begin{array}{l}\rightarrow CHO{-}CHO\\ \rightarrow CH_2OH{-}CHO\end{array} + HCl \xrightarrow{(O)} COOH{-}COOH$$

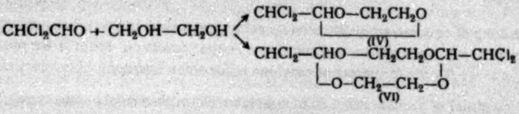
The hydrogen chloride which was then evolved formed ethylene chlorohydrin with ethylene glycol [3] which then reacted with chlorine according to the equation

$$\underset{(I)}{CH_2Cl{-}CH_2OH} + Cl_2 \rightarrow \underset{(II)}{CH_2Cl{-}CHO} + HCl$$

Chloroacetaldehyde could also be formed according to the equation

$$CH_2OH{-}CHO + HCl \rightarrow CH_2Cl{-}CHO + H_2O$$

Chlorination of chloroacetaldehyde took place simultaneously to dichloroacetaldehyde which in the presence of water was oxidized to dichloroacetic acid. Dichloroacetic acid and ethylene chlorohydrin formed an ester which could be further chlorinated. In the presence of mineral acids the carbonyl compounds easily formed cyclic acetals and ketals with vicinal glycols [4].


CHCl$_2$CHO + CH$_2$OH—CH$_2$OH
CHCl$_2$—CHO—CH$_2$CH$_2$O
(IV)
CHCl$_2$—CHO—CH$_2$CH$_2$OCH—CHCl$_2$
O—CH$_2$—CH$_2$—O
(VI)

## EXPERIMENTAL

Chlorination of ethylene glycol. In a quartz reaction vessel fitted with a thermometer and reflux condenser was placed 346 g of ethylene glycol with b.p. 187.5-188.5° and $n^{20}D$ 1.4312. Dry chlorine was introduced through a bubbler of porous glass plate. The reaction vessel had a quartz mercury source PRK-2 placed at a distance of 9 cm. During the chlorination the temperature rose to 127°. The reaction was considered to be complete when increase in weight stopped. Chlorination lasted 14-16 hours. When the liquid stood, it separated and precipitated colorless crystals of oxalic acid in the amount of 15 g with m.p. 101.5° (from ether). Found %: C 19.38; H 4.50. M 130.7, 129.6 (according to Rast). $C_2H_2O_4 \cdot 2H_2O$. Calculated %: C 19.05; H 4.76. M 126.

A mixed melting point with oxalic acid dihydrate showed no depression. In the filtrate we determined by the Fischer reagent 77 g of water, the greater part of which could be removed over ignited $Na_2SO_4$. To remove HCl, dry nitrogen was passed through the product. The substances carried off by the nitrogen were caught in a trap filled with acetone and solid carbon dioxide. For more complete uptake of HCl the product was kept for a long time over calcium carbonate. As a result we obtained 395.6 g of liquid. The data on distillation are given in the Table.

Results of the Distillation of the Product from the Chlorination of Ethylene Glycol in Ultraviolet Light

| Fraction | B. p. (pressure in mm) | Wt. (in g) | $n^{20}_D$ |
|---|---|---|---|
| A | 97—107° (760) | 130.0 | 1.4425 |
| B | 55— 74 (4) | 23.0 | 1.4660 |
| C | 74— 78 (4) | 101.0 | 1.4711 |
| D | 78—150 (4) | 28.0 | 1.4711 |
| E | 150—170 (3) | 55.0 | 1.4959 |
| Residue | | 31.0 | |
| | | 368.0 | |

Fraction A is mixed with water; the remaining fractions are unmixed.

Fraction A contained ethylene chlorohydrin, dichloroacetaldehyde, and water. Since the azeotropic mixture ethylene chlorohydrin—water has a boiling point lying close to those of dichloroacetaldehyde hydrate and water, they could not be separated by distillation, and so their separation was carried out from the mixture. The amount of water, determined by the Fischer method, was 43 g. Hydrogen chloride was removed from 30 g of fraction A by NaOH to give 3.5 g of ethylene oxide. When we formed a derivative of (II) with phenylhydrazine, instead of the expected phenylhydrazone [5] there was formed an osazone hydrochloride (III) analogous to the reaction of (II) with hydroxylamine hydrochloride [6]. From 10 g of fraction A we obtained 3.5 g of (III) with a m.p. 233-234° (from alcohol).

A mixed melting point with the osazone hydrochloride obtained from dichloroacetaldehyde synthesized from trichloroacetic acid [7] showed no depression.

Found %: C 53.38; H 5.61; Cl 23.08; N 18.20. $C_{14}H_{16}N_4Cl_2$. Calculated %: C 54.00; H 5.15; Cl 22.82; N 18.00.

Preliminary study of fraction B showed that it approached the composition of an acetal. Since the acetal was stable to alkali, its separation was made easier by treating the liquid with alkali to free it from esters of ethylene chlorohydrin which were present. 23 g of fraction B, 10 g NaOH and 50 ml of water were boiled 2 hours under reflux, then extracted with ether. As a result we obtained 10 g of 2-dichloromethyl-1,3-dioxolane (IV). After repeated distillations, substance (IV) was isolated.

B. p. 69-72° (9 mm), $n^{20}D$ 1.4754, $d^{20}_4$ 1.4147, $MR_D$ 31.46; calc. 31.49.
According to [8]: b.p. 185-188°.
Found %: C 30.46; H 3.06; Cl 45.47. M 158.4 (cryoscopic). $C_4H_6O_2Cl_2$. Calculated %: C 30.57; H 3.82; Cl 45.22. M 157.

2 g of (IV) and 4.6 g of concentrated hydrochloric acid were boiled under reflux until the layers disappeared, and the mixture was then put over calcium carbonate to a neutral reaction. From it we obtained 2.9 g of (III) and we detected (I) qualitatively (by the formation of ethylene oxide when hydrogen chloride was removed).

Fraction C consisted of β-chloroethyl dichloroacetate (V) with a small admixture of the free acid. From 10.8 g of this fraction we obtained 1.5 g of the aniline salt of dichloroacetic acid with m.p. 123-124° (from benzene with alcohol).

Found %: C 42.50; H 3.69; Cl 31.40; N 5.86. Equiv. 222, 223. $C_8H_9O_2NCl_2$. Calculated %: C 43.24; H 4.05; Cl 31.98; N 6.30. Equiv. 222.

A mixed m.p. with the aniline salt of dichloroacetic acid synthesized from chloral [9] showed no depression. Repeated distillation of the remaining 90 g of fraction C gave 83 g (V).

B.p. 79-82° (7 mm), $n^{20}D$ 1.4722.
According to [10]: b.p. 209-212°.
Found %: C 24.68; H 2.01; Cl 54.78. M 196.4, 195.2 (cryoscopic). $C_4H_5O_2Cl_3$. Calculated %: C 25.06; H 2.61; Cl 55.61. M 191.5.

Saponification of 72 g of (V) by NaOH solution gave 6.8 g of ethylene oxide and 26.8 g of dichloroacetic acid.

Fraction D was not identified; it consisted of a mixture of esters formed by deeper chlorination, with very similar boiling points, and so it was impossible to separate individual substances by distillation.

Fraction E treated like fraction B gave 37 g of acetal (VI). After two distillations we obtained substance (VI).

B.p. 166-170° (3 mm), $n^{20}D$ 1.4910, $d^{20}_4$ 1.4552, $MR_D$ 62.29; calc. 62.98.
Found %: C 30.99; H 3.42; Cl 45.12. M 313 (cryoscopic) $C_8H_{12}O_4Cl_4$. Calculated %: C 30.57; H 3.82; Cl 45.22. M 314.

Splitting with concentrated hydrochloric acid, as with (IV), gave, from 1.6 g of (VI), 3.1 g of (III), and (I) was detected qualitatively.

Chlorination of β-chloroethyl dichloroacetate. 48.5 g of β-chloroethyl dichloroacetate (V) (b.p. 75-78° at 3 mm, $n^{20}D$ 1.4707) was isolated from the chlorination product of ethylene glycol and purified by distillation three times; it was chlorinated under conditions analogous to those for chlorination of ethylene glycol. The temperature did not rise above 34°. After 45 hours, increase in weight stopped. It was freed from HCl as ethylene glycol had been. As a result we obtained 78.5 g of chlorination product. By twice redistilling we isolated 30 g of α,β,β',β''-tetrachloroethyl trichloroacetate (VII).

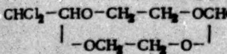
B.p. 90-92° (2 mm), $n^{20}_D$ 1.4991, $d^{20}_4$ 1.6966, $MR_D$ 56.73; calc. 56.39. Found %: C 14.61; H 0.55; Cl 74.97. M 327. (cryoscopic). $C_4HO_2Cl_7$. Calculated %: C 14.56; H 0.30; Cl 75.41. M 329.5.

From 8.5 g of (VII) by ammonolysis we obtained 2.3 g of a substance with m.p. 138° (sublimation) which gave no depression by mixed melting point with trichloroacetamide.

Chlorination of ethylene glycol in the presence of $SbCl_5$. When ethylene glycol was chlorinated with the addition of 0.2% $SbCl_5$ there was energetic reaction with evolution of heat, and the temperature reached a maximum of 110°. The original weight increased by 50-60%. The chlorination product was treated like the chlorination product in ultraviolet light. Altogether, the following substances were found HCl, $H_2O$, $(COOH)_2 \cdot 2H_2O$, $CHCl_2CHO$, $CHCl_2COOH$, $CHCl_2CHO-CH_2-CH_2O$ and $CHCl_2-COOCH_2CH_2Cl$.

## SUMMARY

1. We have studied the chlorination of ethylene glycol initiated by ultraviolet light. We have isolated and identified the following products: β-chloroethyl dichloroacetate (27%), an acetal of the structure



$CHCl_2-CHO-CH_2-CH_2-OCHCHCl_2$ with $-OCH_2-CH_2-O-$ below

(15%), water (12%), dichloroacetaldehyde (11%), ethylenechlorohydrin (11%), 2-dichloromethyl-1,3-dioxolane (6%), and admixtures of oxalic and dichloroacetic acids. We have found that when ethylene glycol is chlorinated in the presence of $SbCl_5$ the same products are formed, except for the second.

2. We have shown that when β-chloroethyl dichloroacetate is chlorinated in ultraviolet light, $\alpha,\beta,\beta',\beta''$-tetrachloroethyl trichloroacetate is obtained in 62% yield.

## LITERATURE CITED

[1] M. Mitscherlich, Comptes rend. 56, 188 (1863).

[2] L. Donciu, Monatsh. 16, 1 (1895).

[3] Würtz, Ann. Chim. (3) 55, 418 (1859).

[4] A. C. Neish and F. J. MacDonald, Can. J. Research, 25, 75, 423 (1947).

[5] R. Schriner and R. Fuson, Systematic Qualitative Analysis of Organic Compounds 121 (1950).*

[6] O. Routala and W. Neovius, Ber. 57, 252 (1924).

[7] E. Reisse, Lieb. Ann. 257, 331 (1890).

[8] M. J. Astle and J. A. Zaslowsky and P. G. Lafyatis, Ind. Eng. Ch. 46, 787 (1954).

[9] M. Delepine, Bull. Soc. Chim. (4) 45, 827 (1929).

[10] Delacre, Bull. Soc. Chim. (2) 48, 708 (1887).

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*In Russian.

# STUDIES IN THE FIELD OF GLYCOL ETHERS AND THEIR DERIVATIVES

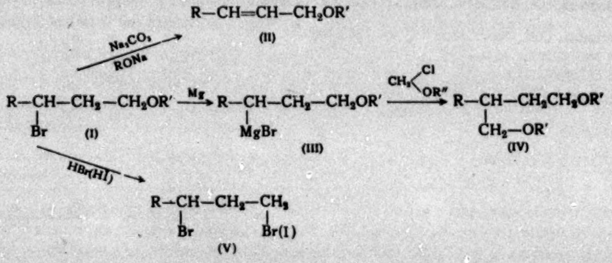
## XXXIII. SOME CHEMICAL TRANSFORMATIONS OF γ-BROMOETHERS OF THE ALIPHATIC SERIES

Shamkhal Mamedov and B. K. Zeinalov

It was shown earlier that γ-bromoethers are easily obtained by alkylation of α-bromoethers by ethylene hydrocarbons [1]. It is interesting to investigate some chemical transformations of the γ-bromoethers, which, according to the literature, are almost unknown [2, 3].

Experiments on the hydrolysis of γ-bromoethers (I) carried out in the presence of $Na_2CO_3$ and $CaCO_3$ (10-12 hours) showed that HBr was then split out with the formation of ethers of allyl alcohol homologs (II). In all cases, instead of the expected product, the partial ethers of the β-glycols, we obtained unsaturated ethers. When the γ-bromoethers were heated with a solution of alcoholic alkali, the splitting out of HBr ended much sooner (2-3 hours). When sodium alcoholate acted on these bromoethers (I), instead of the expected etherification reaction, there occurred splitting out of HBr with formation of the allyl ethers (II). The order of splitting out of HBr agreed with the Markovnikov rule, which was shown by establishing the structures of the allyl ethers by oxidation [1].

The negative results of the hydrolysis and etherification reactions are evidently due to some mobility of the hydrogen in the β-position with respect to the oxygen bridge in the γ-haloethers (I); on the other hand, the presence of bromine on the secondary carbon atom apparently makes the splitting out of HBr easier. γ-Bromoethers (I) like γ-chloroethers [1] easily give magnesium organic compounds (III) which can react with α-chloroethers to form 1,4-glycol ethers (IV). In this way a new possibility has been discovered for the synthesis of glycol ethers with different alkoxy groups in the 1,4-positions (IV).



γ-Bromoethers (I), like γ-chloroethers [1], under the action of HBr or HI form the corresponding 1,3-dihalo derivatives (V). In this way we synthesized and studied 6 new examples of 1,3-dihalo derivatives of saturated hydrocarbons whose constants are given in the Table.

Constants of 1,3-Dihalo Derivatives

| No. | Structural formula $R{-}CH(X){-}CH_2{-}CH_2(Y)$ |  |  | Name of dihalogen compound | Boiling point (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ |  | $M$ |  | Halogen content (in %) |  | Yield (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  | R | X | Y |  |  |  |  | found | calc. | found | calc. | found | calc. |  |
| 1 | $CH_3$ | Br | I | 1-Iodo-3-bromobutane $C_4H_8BrI$ | 66—67° (15) | 1.9600 | 1.5340 | 41.71 | 41.23 | 269.7 | 263.0 | 77.81 | 78.54 | 76.4 |
| 2 | $CH_3$ | Cl | Br | 1-Bromo-3-chlorobutane $C_4H_8ClBr$ | 45—47 (12) | 1.4503 | 1.4736 | 33.21 | 33.30 | 172.9 | 171.5 | 67.17 | 67.34 | 75.8 |
| 3 | $CH_3$ | Cl | I | 1-Iodo-3-chlorobutane $C_4H_8ClI$ | 52—54 (5) | 1.7500 | 1.5230 | 38.14 | 38.33 | 220.7 | 218.5 | 74.61 | 74.37 | 68.7 |
| 4 | $C_2H_5$ | Br | I | 1-Iodo-3-bromopentane $C_5H_{10}BrI$ | 84—86 (18) | 1.8332 | 1.5290 | 46.63 | 45.86 | 281.6 | 277.0 | 75.28 | 74.73 | 79.3 |
| 5 | $C_2H_5$ | Cl | Br | 1-Bromo-3-chloropentane $C_5H_{10}ClBr$ | 53—55 (10) | 1.3900 | 1.4734 | 37.46 | 37.92 | 188.3 | 185.5 | 61.98 | 62.26 | 81.1 |
| 6 | $C_2H_5$ | Cl | I | 1-Iodo-3-chloropentane $C_5H_{10}ClI$ | 55—57 (5) | 1.6600 | 1.5200 | 42.58 | 42.95 | 234.2 | 232.5 | 70.17 | 69.89 | 81.9 |

These chemical transformations indicate the possibility of the synthesis of a series of organic compounds whose starting substances can be the products of alkylation of γ-bromoethers by ethylene hydrocarbons, especially 1,3-dihalo derivatives of hydrocarbons which contain not only the same, but also different halogens in the molecule.

## EXPERIMENTAL

Action of an aqueous soda solution on butyl bromobutyl ether (I, R = $CH_3$, R' = n-$C_4H_9$). To a solution of 15 g of $Na_2CO_3$ in 150 ml of water was added 20.9 g of the bromoether (I) and the resulting mixture was heated for 15 hours. The reaction product was extracted with ether. After drying and distilling off the solvent, a vacuum distillation gave 6 g (45%) of butyl γ-methylallyl ether (II, R = $CH_3$, R' = n-$C_4H_9$).

B.p. 154-156°, $d^{20}_{20}$ 0.8100, $n^{20}D$ 1.4150, $MR_D$ 39.57. $C_8H_{16}F$. Calculated 40.32.
Found M 125. Calculated 128.

The position of the double bond in the allyl ethers obtained from γ-haloethers was shown by oxidation [1].

Under analogous conditions $Na_2CO_3$ was replaced by $CaCO_3$ and in this case the same splitting out of HBr occurred.

Thus, for example, by heating a mixture of 16.7 g of methyl γ-bromobutyl ether (I, R = R' = $CH_3$) and 15 g of chemically pure $CaCO_3$ with 150 ml of water for 14 hours we obtained 3.5 g (40%) of methyl γ-methylallyl ether (II, R = R' = $CH_3$).

B.p. 78-81°, $d^{20}_{20}$ 0.7972, $n^{20}D$ 1.4010, $MR_D$ 26.21. $C_5H_{10}F$. Calculated 26.46.
Literature data [4]: b.p. 79°, $d^0$ 0.8035.

Action of alcoholic alkali on methyl γ-bromoamyl ether (I, R = $C_2H_5$, R' = $CH_3$). A mixture of 18 g of bromoether, 5.6 g of KOH and 10 ml of 95% ethyl alcohol was heated on the water bath for 3 hours. After the usual treatment we obtained 6.5 g (56%) of methyl γ-ethylallyl ether (II, R = $C_2H_5$, R' = $CH_3$).

B.p. 103-106°, $d^{20}_{20}$ 0.7910, $n^{20}D$ 1.4030, $MR_D$ 30.35. $C_6H_{12}OF$. Calculated 31.08.
Found M 102.1. Calculated 100.

Action of sodium ethylate on butyl γ-bromoamyl ether (I, R = $C_2H_5$, R' = n-$C_4H_9$). 2.3 g of metallic sodium was dissolved in 8 g of anhydrous alcohol and then 22.3 g of γ-bromoether was added to the mixture and the reaction flask was heated for

4 hours on the water bath; then water was added to the flask and the product was extracted by ether. After drying and distilling off the solvent, vacuum distillation gave 8 g (55%) of butyl γ-ethylallyl ether [1] (II, R = $C_2H_5$, R' = = n-$C_4H_9$).

B.p. 169-172°, $d^{20}_{20}$ 0.8090, $n^{20}D$ 1.4200, $MR_D$ 44.42. $C_9H_{18}O$F. Calculated 44.93.

*Action of α-chloroethers on the magnesium organic compounds prepared from γ-bromoether (I).* From 2.4 g of magnesium and 18.2 g of butyl α-bromobutyl ether (I, R = $C_2H_5$, R' = n-$C_4H_9$) we prepared the magnesium organic compound (III) by the method described in previous work [1]. Then the resulting Grignard reagent we added 12.3 g of α-chloromethyl ether. The reaction flask was heated on the water bath with stirring for 1 hour. After the usual treatment we obtained 6 g of 2-ethyl-1-methoxy-4-butoxybutane (IV, R = $C_2H_5$, R' = n-$C_4H_9$, R" = $CH_3$).

B.p. 205-208°, $d^{20}_{20}$ 0.8540, $n^{20}D$ 1.4200, $MR_D$ 55.71. $C_{11}H_{24}O_2$. Calculated 56.28. Found M 183. Calculated 188.

The structure of the resulting ether was established by the action of HBr on it: 5 g of the ether was saturated with gaseous HBr at −10° and heated in a sealed tube at 100° for 12 hours. Vacuum distillation gave 5 g of 2-ethyl-1,4-dibromobutane.

B.p. 84-86° (12 mm), $d^{20}_{20}$ 1.6510, $n^{20}D$ 1.5180, $MR_D$ 44.78. $C_6H_{12}Br_2$. Calculated 45.43.

*Action of HBr on methyl γ-bromoamyl ether (I, R = $C_2H_5$, R' = $CH_3$).* The experiment was carried out as previously described [1]. From 18 g of the γ-bromoether we obtained 20 g of the 1,3-dibromopentane (V, R = = $C_2H_5$).

B.p. 63-65° (10 mm), $d^{20}_{20}$ 1.6683, $n^{20}D$ 1.5066, $MR_D$ 41.00. $C_5H_{10}Br_2$. Calculated 40.82.
Literature data [5]: b.p. 190-195° (750 mm), $d^{20}_4$ 1.6720, $n^{20}D$ 1.5048.

*Action of HI on methyl γ-bromoamyl ether (I, R = $C_2H_5$, R' = $CH_3$).* 18 g of the bromoether was saturated with HI at 0°. The cylinder was closed with a ground glass stopper and kept at room temperature for 36 hours. The reaction mixture was poured into cold water. The lower layer was washed with 2% sodium hydroxide and with water. After drying and vacuum distillation we obtained 18 g of 1-iodo-3-bromopentane, whose constants are given in the Table (substance 4).

In an analogous way, by the action of HBr or HI on γ-bromo- and γ-chloroethers we obtained the other 5 new mixed 1,3-dihalogen derivatives of saturated hydrocarbons whose constants are given in the Table.

## SUMMARY

1. We have shown that when γ-bromoethers are heated with solutions of $Na_2CO_3$, $CaCO_3$, and sodium alcoholate, splitting out of HBr occurs, with formation of allyl ethers.

2. Magnesium organic compounds prepared from γ-bromoethers react smoothly with α-chloroethers with formation of the ethers of 1,4-glycols.

3. We have studied the action of HBr and HI on γ-bromo- and γ-chloroethers. We have shown that this forms 1,3-dihalogen derivatives of saturated hydrocarbons in yields up to 80%.

## LITERATURE CITED

[1] Shamkhal Mamedov, Zh. O. Kh. 27, 1499 (1957).*

[2] A. A. Volkov and B. N. Menshutkin, Zh. R. Kh. O. 30, 559 (1898).

[3] B. N. Menshutkin, Zh. R. Kh. O. 32, 355 (1900).

[4] Charon, Ann. Ch. (7) 17, 255 (1899).

[5] N. A. Riazanov, Zh. R. Kh. O. 48, 179 (1916).

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* Original Russian pagination. See C. B. Translation.

# STUDIES IN THE FIELD OF GLYCOL ETHERS AND THEIR DERIVATIVES.

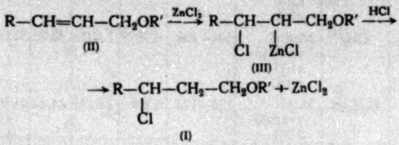
## XXXIV. CHEMICAL TRANSFORMATIONS OF γ-CHLOROETHERS

Shamkhal Mamedov and B. Pishnamazzade

The chemical transformations of γ-chloroethers have been very little studied [1-3]. It was shown earlier [4] that ethers of homologs of allyl alcohol (II), for the synthesis of which the existing methods are not satisfactory [5-8], can be obtained by splitting out HCl from γ-chloroethers (60%). It becomes interesting to make a more detailed study of the properties of the ethers of allyl alcohol homologs (II) which, according to the literature, have hardly been studied.

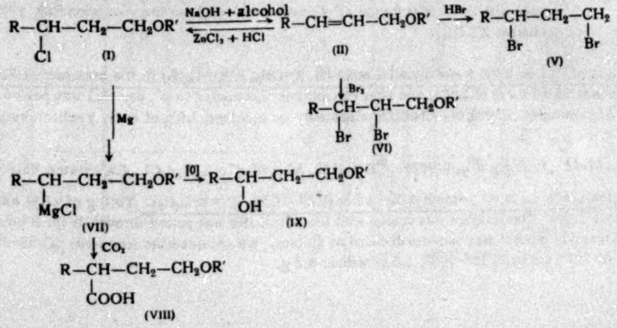
When hydrogen halides act on allyl ethers (II) the double bond of the ether remains untouched and the oxygen bridge is easily broken with the formation of unsaturated (III) and saturated (IV) halogen derivatives of hydrocarbons [9, 10]. However, as our experiments showed, HCl and HBr in the presence of a catalyst ($ZnCl_2$) combine smoothly at the double bond of the allyl ethers even in the cold (at 0°). The reaction product is the corresponding γ-haloether, which we have isolated and identified. Hence, addition of the hydrogen halide occurs in such a way that the hydrogen goes to the carbon nearest the oxygen bridge (according to the Markovnikov rule).

The reaction with the catalyst can be presented by the following scheme, in accord with the work of Kondakov [11].



$$\underset{(II)}{R-CH{=}CH-CH_2OR'} \xrightarrow{ZnCl_2} \underset{(III)}{R-\underset{Cl}{\underset{|}{CH}}-\underset{ZnCl}{\underset{|}{CH}}-CH_2OR'} \xrightarrow{HCl} \underset{(I)}{R-\underset{Cl}{\underset{|}{CH}}-CH_2-CH_2OR'} + ZnCl_2$$

When hydrogen bromide acts on allyl ethers in the presence of $ZnBr_2$, the chief product is the γ-bromoether (V). However, in the case of excess HBr, deeper reaction occurs and there is also formation of a certain amount of 1,3-dibromo derivative of the hydrocarbon.



$$\underset{(I)}{R-\underset{Cl}{\underset{|}{CH}}-CH_2-CH_2OR'} \underset{ZnCl_2\,+\,HCl}{\overset{NaOH\,+\,alcohol}{\rightleftarrows}} \underset{(II)}{R-CH{=}CH-CH_2OR'} \xrightarrow{HBr} \underset{(V)}{R-\underset{Br}{\underset{|}{CH}}-CH_2-\underset{Br}{\underset{|}{CH_2}}}$$

$$(II) \xrightarrow{Br_2} \underset{(VI)}{R-\underset{Br}{\underset{|}{CH}}-\underset{Br}{\underset{|}{CH}}-CH_2OR'}$$

$$(I) \xrightarrow{Mg} \underset{(VII)}{R-\underset{MgCl}{\underset{|}{CH}}-CH_2-CH_2OR'} \xrightarrow{[O]} \underset{(IX)}{R-\underset{OH}{\underset{|}{CH}}-CH_2-CH_2OR'}$$

$$(VII) \xrightarrow{CO_2} \underset{(VIII)}{R-\underset{COOH}{\underset{|}{CH}}-CH_2-CH_2OR'}$$

When bromine acts on allyl ethers (II) in the cold (−15°) it gives β,γ-dibromoethers (VI) in good yield (75%). This method opens many possibilities for obtaining different β,γ-dibromo derivatives of ethers which are suitable for organic syntheses.

Magnesium organic compounds (VII) prepared from γ-chloroethers [4] are easily oxidized by pure oxygen and oxygen of the air. In the latter case oxidation proceeds more moderately and as a result magnesium haloglycolates are obtained, which with water give monoethers of β-glycols (IX) with yields of 10-15%. These Grignard reagents (VII) rapidly absorb carbon dioxide gas with the formation of magnesium salts of hydroxyacid ethers which by further treatment with dilute acids form ethers of γ-hydroxyacids (VIII).

## EXPERIMENTAL

The synthesis of allyl ethers was carried out under the conditions described earlier [4]. The constants for the allyl ethers which were synthesized are given in Table 1.

TABLE 1

Allyl Ethers

| No. | Struct. formula of ethers $R-CH=CH-CH_2OR'$ | | Name of ether | Boiling point | $d^{20}_{20}$ | $n^{20}_D$ | $MR_D$ | | $M$ | | Yield (in %) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | R | R′ | | | | | found | calc. | found | calc. | |
| 1 * | $C_2H_5$ | $C_2H_5$ | Ethyl γ-ethyl-allyl ether | 123—127° | 0.7981 | 1.4093 | 35.34 | 35.70 | 117.2,<br>112.4 | 114.0 | 41.25 |
| 2 ** | $C_2H_5$ | $CH_3$ | Methyl γ-ethyl-allyl ether | 104—108 | 0.7899 | 1.4023 | 30.85 | 31.08 | — | — | 36.4 |
| 3 ** | $C_2H_5$ | $C_4H_9$-n. | Butyl γ-ethyl-allyl ether | 170—174 | 0.8083 | 1.4198 | 44.44 | 44.93 | — | — | 62.35 |

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*First time synthesized. The structure of the allyl ether obtained from the γ-chloroether was shown by oxidation [4].

**Agrees with the results for the allyl ethers obtained from the corresponding γ-bromoethers (paper XXXIII).

Action of HCl on butyl γ-methylallyl ether (II, $R=CH_3$, $R'=n-C_4H_9$) in the presence of $ZnCl_2$. To 4 g of allyl ether was added 0.5 g of $ZnCl_2$ and after the mixture was cooled to 0°, dry HCl was passed through it for 6 hours. After washing, drying, and distilling repeatedly we obtained 0.8 g of butyl γ-chlorobutyl ether (I, $R=CH_3$, $R'=n-C_4H_9$) [4].

B.p. 67-68° (19 mm), $d^{20}_{20}$ 0.9020, $n^{20}D$ 1.4160, $MR_D$ 45.47. $C_8H_{17}OCl$. Calculated 45.65.

Action of HBr on butyl γ-methylallyl ether (II, $R = CH_3$, $R' = n-C_4H_9$). To 3 g of allyl ether was added 0.3 g of anhydrous $ZnBr_2$. The mixture was cooled with ice water, HBr was passed through it for 3 hours, and the washed and dried reaction product was vacuum distilled at 20 mm. We obtained the fractions: 1) 52-69°, 0.5 g; 2) 69-72°, 1.2 g; 3) 72-104°, 0.7 g; 4) 105-109°, 1.5 g; residue 0.8 g.

TABLE 2

β,γ-Dibromoethers

| No. | Structural formula of ethers $R{-}\underset{Br}{CH}{-}\underset{Br}{CH}{-}CH_2OR'$ | | Name of ether | Boiling point (pressure in mm) | $d_{20}^{20}$ | $n_D^{20}$ | $MR_D$ | | $M$ | | Bromine content (in %) | | Yield (in %) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | R | R′ | | | | | found | calc. | found | calc. | found | calc. | |
| 1 | $CH_3$ | $C_4H_9$-n | Butyl β,γ-dibromobutyl ether | 122° (16) | 1.4627 | 1.4880 | 56.74 | 56.31 | 283.5 | 288 | 55.75 | 55.56 | 77 |
| 2 | $C_2H_5$ | $C_4H_9$-n | Butyl β,γ-dibromoamyl ether | 127—128 (16) | 1.4413 | 1.4910 | 60.70 | 60.93 | 297.0 | 302 | 52.58 | 52.98 | 67 |
| 3 | $C_2H_5$ | $C_2H_5$ | Ethyl β,γ-dibromoamyl ether | 120 (20) | 1.4982 | 1.4819 | 52.14 | 51.70 | 272.8 | 274 | 58.42 | 58.39 | 75 |

TABLE 3

Partial Ethers of 1,3-Diols

| No. | Structural formula of ethers $R{-}\underset{OH}{CH}{-}CH_2{-}CH_2OR'$ | | Name of ether | Boiling point (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ | | $M$ | | % C | | % H | | % (OH) | | Yield (in %) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | R | R′ | | | | | found | calc. | found | calc. | found | calc. | found | calc. | found | calc. | |
| 1 | $CH_3$ | $C_2H_5$ | 1-Ethoxy-3-butanol | 175—178° | 0.9051 | 1.4246 | 33.31 | 33.08 | 121.9 | 118 | 61.11 | 61.01 | 11.95 | 11.88 | 15.04 | 14.41 | 15.7 |
| 2 | $C_2H_5$ | $CH_3$ | 1-Methoxy-3-pentanol | 77—82 (23) | 0.9163 | 1.4262 | 33.01 | 33.08 | 120.4 | 118 | 61.41 | 61.01 | 11.81 | 11.88 | 14.31 | 14.41 | 12.3 |
| 3 | $C_2H_5$ | $C_2H_5$ | 1-Ethoxy-3-pentanol | 82—85 (20) | 0.8971 | 1.4223 | 37.41 | 37.69 | 129.5 | 132 | 63.51 | 63.63 | 12.15 | 12.12 | 13.75 | 12.88 | 11.4 |

Fraction 2 was 1,3-dibromobutane:

$d^{20}_{20}$ 1.7756, $n^{20}D$ 1.5092, $MR_D$ 36.36. $CH_8Br_2$. Calculated 36.20 [12].

Fraction 4 was butyl γ-bromobutyl ether (V, R = $CH_3$, R' = n-$C_4H_9$):

$d^{20}_{20}$ 1.1395, $n^{20}D$ 1.4468, $MR_D$ 49.01. $C_8H_{17}OBr$. Calculated 48.55 [4].

Synthesis of β,γ-dibromobutyl ether (VI, R = $CH_3$, R' = n-$C_4H_9$). 2 g of butyl γ-methylallyl ether (II, R = $CH_3$, R' = n-$C_4H_9$) was placed in a test tube and the calculated amount of bromine was added to it dropwise with cooling (−15°) and shaking. After it was washed and dried, the reaction product was vacuum distilled. We obtained 3.5 g (77%) of β,γ-dibromoether (VI, R = $CH_3$, R' = n-$C_4H_9$) (Table 2, substance 1). In an analogous manner we obtained two more new β,γ-dibromoethers whose constants are given in Table 2.

Oxidation of magnesium organic compounds (VII, R = $CH_3$, R' = $C_2H_5$). From 1.8 g of magnesium and 11 g of ethyl γ-chlorobutyl ether (I, R = $CH_3$, R' = $C_2H_5$) was prepared the magnesium organic compound (VII, R = $CH_3$, R' = $C_2H_5$) through which a stream of dry air was passed (14 liters) at 0° for 2.5 hours. The oxidation product was decomposed with dilute hydrochloric acid. After washing, drying, and distilling off the solvent we submitted the product to fractional distillation. We obtained 1.5 g (15.7%) of the monoethyl ether of 1,3-butanediol (Table 3, substance 1). The experiment was repeated with pure oxygen. The yield of monoether was 13.6%.

In an analogous manner we obtained two more monoethers whose constants are given in Table 3.

Action of carbon dioxide on the magnesium organic compound (VII, R = $CH_3$, R' = n-$C_4H_9$). From 2.4 g of magnesium and 16.5 g of butyl γ-chlorobutyl ether (I, R = $CH_3$, R' = n-$C_4H_9$) we prepared the magnesium organic compound in the usual way, and passed through it a stream of dry carbon dioxide gas with cooling (5°). After the usual treatment we obtained 4 g of a liquid with b.p. 141-144° (5 mm), $d^{20}_{20}$ 0.9328, $n^{20}D$ 1.4308. The product had acid properties and by analysis of its silver salt (needles from alcohol) was γ-butoxy-α-methyl butyric acid (VI, R = $CH_3$, R' = n-$C_4H_9$).

Found %: Ag 38.32. $C_9H_{17}O_3Ag$. Calculated %: Ag 38.39.

## SUMMARY

1. We have given a method for the synthesis of β,γ-dibromo derivatives of ethers.

2. We have shown that by the action of HBr and HCl on allyl ethers in the presence of $ZnCl_2$ or $ZnBr_2$ there is an addition reaction with formation of γ-haloethers.

3. We have established that by the oxidation of magnesium organic compounds prepared from γ-chloroethers, monoethers of β-glycols are formed as magnesium halogen alcoholates.

4. We have established that by the action of carbon dioxide on the magnesium organic compounds prepared from γ-chloroethers, ethers of γ-hydroxy acids are formed.

## LITERATURE CITED

[1] English patent 423520 (1933); Zbl.1935, II, 920.

[2] English patent 2024749 (1932); Zbl. 1936, I, 4074.

[3] F. Straus and W. Thiel, Lieb. Ann. 525, 151 (1936).

[4] Shamkhal Mamedov, Zh. O. Kh. 27, 1499 (1957).*

[5] M. Berthelot and R. Luca, Ann. Chim. (3), 43, 292 (1856).

[6] Cahaurs and Hofmann, Lieb. Ann. 102, 290 (1857).

[7] A. M. Butlerov, Zh. R. Kh. O. 2, 187 (1870).

[8] W. Ipatieff, J. pr. Ch. (2), 59, 523 (1899).

[9] Silva, Ber. 8, 1352 (1875).

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*Original Russian pagination. See C. B. Translation.

[10] N. M. Kizhner, Zh. R. Kh. O. 22, 27 (1890).

[11] I. Kondakov, Zh. R. Kh. O. 26, 12 (1894).

[12] N. Ia. Dem'ianov, Zh. R. Kh. O. 39, 1085 (1907).

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# N-DI(CHLOROETHYL)AMINES OF THE ALICYCLIC SERIES. I.

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The search for anti-cancer substances among the nitrogen analogs of yperite [N-di(chloroalkyl)amines] has continued until now. The basic purpose of work in this direction is to find substances with the greatest effectiveness and the lowest toxicity. Investigators have studied aliphatic, aromatic, fatty-aromatic, heterocyclic, and other di(chloroalkyl) amines. Among the alicyclic dichloroalkyl amines only a single example is mentioned in the literature [1].

In the present work we report the synthesis of some of the properties of dichloroalkylamines of the cyclopentane, cyclohexane, and cycloheptane series. We have synthesized compounds of two types: in one (I) the di(chloroalkyl)amine group is connected directly to a ring carbon, in the other to a carbon in the side chain (II).

$$\underset{\text{(I)}}{R{-}N(CH_2CH_2Cl)_2} \qquad \underset{\text{(II)}}{R{-}CH_2N(CH_2CH_2Cl)_2}$$

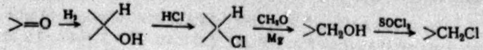
R = cyclopentyl, cyclohexyl, cycloheptyl

Compounds of type (II) are alicyclic derivatives of methyl N-bis-(chloroethyl)-amine (Soviet embichine) which has some value in oncology.

For the synthesis of N-di(chloroethyl)amines we have applied two very useful methods which differ from each other in the means of obtaining the intermediate N-di(hydroxyethyl)amine $RN(CH_2CH_2OH)_2$. In one process (a) (see Table 1), ethylene oxide acts on the amino compound; in the other (b) a halogen-containing compound is introduced into reaction with the diethanol amine. The conditions of carrying out the final step are the same for both methods; the replacement of the hydroxyl group by chlorine depends on the specific properties of N-di(hydroxyethyl)amine.

To obtain N-di(chloroethyl)amines of type (I) by method (b) the halogen in the alicyclic compound is not sufficiently reactive, since under various conditions, even including the use of high pressures, temperatures, and catalysts, only the starting halogen compound was recovered. Therefore the synthesis of dichloroalkylamines of this type was carried out by method (a). The required starting alkylamines were obtained in the cyclopentane and cycloheptane series by reducing the oximes of the corresponding ketones [2], and in the cyclohexane series by catalytic hydrogenation of the aromatic amino compounds. The hydrogenation was carried out in the presence either of Raney nickel or of platinum prepared by the Adams method. We hydrogenated aniline, p-aminobenzoic acid, its ethyl ester, m-aminobenzoic acid, and 1,3-phenylenediamine. The description of the hydrogenation of these compounds in the presence of nickel or platinum catalysts of different types is found in the literature [3], but in spite of this we had either to select the reaction conditions again or change the literature descriptions. When we hydrogenated in the presence of Raney nickel at high temperatures and pressures we found a cracking effect with liberation of ammonia. The amount of hydrogen absorbed usually exceeded the theoretical calculation. The yield of hydrogenated compounds was low. When we hydrogenated the same aromatic amino compounds in the presence of platinum (introduced into the reaction as platinum oxide), side reactions were not found. In the presence of a platinum catalyst we obtained ethyl 1,4-aminocyclohexanecarboxylate, 1,4- and 1,3-aminocyclohexanecarboxylic acids, and 1,3-cyclohexylenediamine. We did not attempt to determine the stearic structure of these compounds and in further reactions we used the mixture of stereoisomers obtained by hydrogenation. The preparation of 1,3-cyclohexylenediamine allowed us to introduce two N-di(chloroethyl)amine groups into the cyclohexane molecule, which was of interest for the biological studies.

For carrying out the synthesis of compounds of type (II) we used as starting substances the chloromethyl derivatives of the same alicyclic hydrocarbons. The chloromethylcycloalkanes were obtained by the following scheme.



(1) (2) (3) (4)

In the cyclopentane and cycloheptane series the syntheses were carried out beginning with the reduction of the ketone (1), in the cyclohexane series by obtaining chlorocyclohexane. Among the many and varied methods for reducing cyclopentanone [4] to cyclopentanol described in the literature the most suitable seemed to be hydrogenation in the presence of Raney nickel. The hydrogenation was carried out under more vigorous conditions than those of the literature; we used the same process for reduction of cycloheptanone. In this and other cases the cycloalkanols were obtained with yields of 67-87%. The remaining steps in the synthesis (2-3-4) were carried out as described in the literature [5]. In the cycloheptane series steps (3) and (4) were carried out for the first time. The reaction of replacement of chlorine by the di(hydroxyethyl)amine group in the chloromethylcycloalkanes by the action on them of diethanol amine was possible, but occurred only on long heating in a sealed tube and with addition of triethylamine to the reaction mixture. N-di (hydroxyethyl)amines, independent of their method of preparation, were in most cases introduced into the next reaction after one distillation in a vacuum.

The replacement of the hydroxyl by chlorine in N-di(hydroxyethyl)amines of both types (I and II) was carried out with thionyl chloride. This reaction occurred in the cold or at room temperature; heating caused strong tarring of the substances. The use of this method directly for 1,3- and 1,4-aminocyclohexanecarboxylic acids did not give good results, and so their di(chloroethyl) derivatives were obtained by saponifying the ethyl esters of 1,3- and 1,4-di(chloroethyl)aminocyclohexanecarboxylic acids. The latter were obtained in the usual way.

The N-di(chloroethyl)amines which we obtained are shown in Table 2 and the results of their biological study will be published in another place. According to preliminary results (A. I. Kravchenko) the most active and least toxic are the N-di(chloroalkyl)amines of the cycloheptane series, which certainly gives a reason for further search in this series for anti-cancer substances.

## EXPERIMENTAL

Cyclohexylamine. In a rotating autoclave was placed 50 g of aniline and 10 g of Raney nickel,* the autoclave was filled with hydrogen to a pressure of 110 atm and heating was begun; at 160-170° and a hydrogen pressure of 140-150 atm rapid absorption of hydrogen occurred. After the corresponding treatment we obtained 16.85g (31%) of cyclohexylamine with b.p. 130-140°. The fraction which boiled above 140° crystallized on standing; the resulting substance melted at 90-100° which corresponds to the melting point of diphenylamine.

Ethyl 1,4-aminocyclohexanecarboxylate.** a) In the autoclave was placed 10 g of ethyl p-aminobenzoate hydrochloride, 150 ml of distilled water, and 1.5 g of platinum oxide. The autoclave was filled with hydrogen to a pressure of 50 atm and hydrogenation was carried out at room temperature (20°). At the end of the reaction the catalyst was separated, the water was distilled off in a vacuum, and the remaining substance was treated with a soda solution; the oil which separated was removed, dried and distilled in a vacuum, b. p. 125-135° (20-23 mm).

Found %: N 8.23. $C_9H_{17}O_2N$. Calculated %: N 8.17.

b) A mixture of 1,4-aminocyclohexanecarboxylic acid and a 15% ethyl alcohol solution of hydrogen chloride was heated. After the usual treatment we obtained the ethyl 1,4-aminocyclohexanecarboxylate with b.p. 125°

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*The hydrogenation of aniline in the presence of nickel oxide is described in the literature [6].

**In the literature the hydrogenation of p-aminobenzoic and m-aminobenzoic acids in the presence of platinum is described. The hydrogenation is carried out without increased pressure [3].

(20 mm), $n^{20}D$ 1.4640. Yield 45%.

1,3-Aminocyclohexanecarboxylic acid and its ethyl ester. 6 g of m-aminobenzoic acid, 0.75 g of platinum oxide, and 80 ml of distilled water were placed in an autoclave for hydrogenation. Hydrogenation was carried out at room temperature; the original hydrogen pressure was 80 atm.

The reaction lasted for 4 hours. We obtained 6.44 g of substance with m.p. 251-252°. The substance was used without further purification for obtaining the ethyl ester.

The ethyl ester was obtained by heating 1,3-aminocyclohexanecarboxylic acid with a 15% solution of hydrogen chloride in anhydrous ethyl alcohol. B.p. 120-125° (15 mm), $n^{20}D$ 1.4640. Yield 75%.

Found %: C 62.88; H 10.03. $C_9H_{17}O_2N$. Calculated %: C 63.15; H 10.00.

1,3-Cyclohexylenediamine. In a rotating autoclave with a glass thermometric enclosure was placed 10.8 g of m-phenylenediamine dihydrochloride, 0.78 g of platinum oxide, and 45 ml of water. Hydrogenation was carried out at an initial hydrogen pressure of 50 or 60 atm and at room temperature (20°). Absorption of hydrogen lasted 15 hours and the amount absorbed corresponded to that calculated theoretically. After separation of the catalyst and evaporation of the solvent 34 g of calcium oxide and 123 ml of anhydrous alcohol were added to the residue and the reaction mixture was boiled; the alcohol was distilled off and the residue was repeatedly extracted with ethyl acetate. The ethyl acetate was distilled off and the residue distilled several times in a vacuum. We obtained about 2 g of substance with b.p. 97° (30 mm), $n^{20.5}D$ 1.5205.

Cycloheptanol* 50 g of cycloheptanone** in 100 ml of anhydrous methanol was hydrogenated in an autoclave at a hydrogen pressure of 60 atm and a temperature of 130-140° in the presence of 5 g of catalyst (Raney nickel). Hydrogen absorption lasted 2 hours. After separation of the catalyst and distillation of the alcohol the remaining substance was distilled in a vacuum. We obtained 25 g of cycloheptanol with b.p. 79-82° (12 mm).

Cycloheptyl carbinol. 4.4 g of chlorocycloheptane, 7.5 g of magnesium, and 30 ml of anhydrous ether were first heated with the addition of a little iodine and without stirring. After the reaction had begun, 33.6 g of chlorocycloheptane in 50 ml of ether was gradually added with stirring; when the reaction stopped at room temperature, it was heated for 15-20 minutes. Then, in a stream of nitrogen, 20 g of gaseous paraform was introduced. (The reaction took about half an hour.) Then the contents of the flask were poured on 150 g of ice and 57 ml of 30% sulfuric acid was carefully added. The cycloheptyl carbinol from the reaction mass was steam distilled off, separated, dried, and vacuum distilled, b.p. 84-94° (8-9 mm). We obtained 40 g.

Found %: C 75.00, 74.30; H 12.08, 12.57. $C_8H_{16}O$. Calculated %: C 75.00; H 12.50.

Chloromethylcycloheptane. To a mixture of 27 g of cycloheptyl carbinol and 20 ml of dry chloroform was added a solution of 35 ml of thionyl chloride in 20 ml of chloroform. The mixture was heated 3 hours at the boiling point. The excess thionyl chloride and chloroform were distilled off; the residue was vacuum distilled. We obtained 25 g of substance with b.p. 62-72° (8-10 mm). The substance was not purified more carefully.

Found %: Cl 21.0. $C_8H_{15}Cl$. Calculated %: Cl 24.2.

The substance was used without further purification of the next reaction with diethanol amine.

Preparation of N-di(β-hydroxyethyl)amines. a) A mixture of 1 mole of alicyclic amine and 2 moles of ethylene oxide was heated for 5 hours in a sealed tube in a rocking oven at 120-140°. A little mobile, thick oil was obtained which was either vacuum distilled or was used without distillation for the next reaction.

b) A mixture of 0.98 mole of diethanol amine, 1 mole of chloromethylcycloalkane, and 1 mole of triethylamine was heated 8-9 hours in a rocking oven in a sealed tube at 180-200°. At the end of the heating the N-di(hydroxyethyl)amine was extracted by ether, the ether solution was shaken with charcoal, and the ether was distilled off. The residue was vacuum distilled.

Preparation of N-di(β-chloroethyl)amines. A solution of 1 mole of N-di-(hydroxyethyl)amine and 6 moles of thionyl chloride in chloroform was stirred at room temperature for 8 hours, the thionyl chloride and chloroform

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*Cycloheptanol was previously obtained from cycloheptanone by V. V. Markovnikov [7] by reduction with sodium and alcohol.

**Cycloheptanone was obtained by isomerization of cyclohexanone with diazomethane [8].

TABLE 1

| R | Method of preparation | Empirical formula | Boiling point (pressure in mm) | Analysis (in %) |  |  |  |  |  |
|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  | Calculated |  |  | Found |  |  |
|  |  |  |  | C | H | N | C | H | N |
|  |  |  | $R—N(CH_2CH_2OH)_2$ |  |  |  |  |  |  |
| $C_5H_9$ | a | $C_9H_{19}O_2N$ | 152—154° (6) | — | — | 8.15 | — | — | 8.5 |
| $C_6H_{11}$ | a | $C_{10}H_{21}O_2N$ | 150 (15) | 64.2 | 11.5 | 7.5 | 64.50 | 11.25 | 6.80 |
| $C_6H_{10}(COOC_2H_5)$ (1,4) | a | $C_{13}H_{25}O_4N$ | 166—166.5 (0.25) | 60.2 | 9.7 | 5.40 | 60.20 | 9.74 | 5.28 |
| $C_6H_{10}(COOC_2H_5)$ (1,3) | a | $C_{13}H_{25}O_4N$ | 170—175 (4) | 60.2 | 9.7 | 5.40 | 60.59 | 9.50 | 6.11 |
| $C_7H_{13}$ | a | $C_{11}H_{23}O_2N$ | 173—183 (4) | 65.7 | 11.44 | 6.95 | 65.2 | 11.41 | 6.86 |
| $C_7H_{13}—CH_2$ | b | $C_{12}H_{25}O_2N$ | 140—180 (8—10) | 67.0 | 11.6 | 6.52 | 65.87 | 11.29 | 6.32 |
|  |  |  | $R[N(CH_2CH_2OH)_2]_2$ |  |  |  |  |  |  |
| 1,3-$C_6H_{10}$ | a | $C_{14}H_{30}O_4N_2$ | 252—254 (11) | — | — | 9.64 | — | — | 9.95 |

Note: Cyclopentylmethyl di(hydroxyethyl)amine $C_5H_9CH_2N(CH_2CH_2OH)_2$ and cyclohexylmethyl di(hydroxyethyl)amine were introduced into the following reactions without preliminary distillation and analysis.

TABLE 2

| No. | R | Empirical formula | Melting point | Solvent for recrystallization | Analysis (in %) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Calculated | | | | Found | | | |
| | | | | | C | H | N | Cl | C | H | N | Cl |
| | | $R—N(CH_2CH_2Cl)_2 \cdot HCl$ | | | | | | | | | | |
| 1 | $C_5H_9$ | $C_9H_{17}NCl_2 \cdot HCl$ | 106—107° | Benzene | 43.8 | 7.3 | 5.7 | 43.2 | 43.64 | 7.00 | 5.75 | 43.48 |
| 2 | $C_6H_{11}$ | $C_{10}H_{19}NCl_2 \cdot HCl$ | 175—176 | Acetone + + alcohol | 46.05 | 7.67 | 5.37 | 40.87 | 45.90 | 7.63 | 5.50 | 40.65 |
| 3 | $1,4\text{-}C_2H_5OOCC_6H_{10}$ | $C_{13}H_{23}O_2NCl_2 \cdot HCl$ | 175—176 | Benzene + + alcohol | 46.95 | 7.27 | 4.21 | 32.0 | 47.09 | 7.44 | 4.37 | 32.28 |
| 4 | $1,3\text{-}C_2H_5OCOC_6H_{10}$ | $C_{13}H_{23}O_2NCl_2 \cdot HCl$ | 133—135 | Benzene | 46.95 | 7.27 | 4.21 | 32.00 | 47.14 | 7.2 | 4.77 | 33.39 |
| 5 | $1,4\text{-}HOOC—C_6H_{10}$ | $C_{11}H_{19}O_2NCl_2 \cdot HCl$ | 157—160 | Anhydrous ether* | 43.41 | 6.63 | 4.50 | 34.95 | 43.19 | 6.63 | 4.50 | — |
| 6 | $1,3\text{-}HOOC—C_6H_{10}$ | $C_{11}H_{19}O_2NCl_2 \cdot HCl$ | 68 (decomp.) | Anhydrous ether | 43.41 | 6.63 | 4.50 | 34.95 | 42.96 | 6.65 | 4.61 | 35.06 |
| 7 | $C_7H_{13}$ | $C_{11}H_{21}NCl_2 \cdot HCl$ | 178 | Benzene + + alcohol | 48.2 | 8.04 | 5.1 | 38.8 | 48.11 | 7.92 | 5.01 | 38.51 |
| 8 | $C_5H_9CH_2$ | $C_{10}H_{19}NCl_2 \cdot HCl$ | 128—130 | Ethyl acetate | 46.1 | 7.69 | 5.38 | 40.8 | 45.99 | 7.79 | 5.70 | 40.4 |
| 9 | $C_6H_{11}CH_2$ | $C_{11}H_{21}NCl_2 \cdot HCl$ | 145—147 | Benzene + + alcohol | 48.2 | 8.04 | 5.1 | 38.8 | 48.12 | 7.73 | 5.04 | 38.66 |
| 10 | $C_7H_{13}CH_2$ | $C_{12}H_{23}NCl_2 \cdot HCl$ | 141—143 | Benzene + + alcohol | 49.8 | 8.32 | 4.85 | 37.0 | 49.57 | 8.25 | 4.84 | 36.32 |
| | | $R[N(CH_2CH_2Cl)_2]_2 \cdot 2HCl$ | | | | | | | | | | |
| 11 | $1,3\text{-}C_6H_{10}$ | $C_{14}H_{26}N_2Cl_4 \cdot 2HCl$ | 101 | Chloroform ** | 38.5 | 6.47 | 6.41 | 48.70 | 39.37 | 6.69 | 7.00 | 46. 13 |

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*Substances 5 and 6 were purified by washing with anhydrous ether and drying in a vacuum desiccator over phosphorus pentoxide.

**Purification of this substance was carried out by boiling its chloroform solution with charcoal and after separating the charcoal, distilling the solvent.

were distilled off in a vacuum, and the residue was recrystallized from organic solvents. The N-di(hydroxyethyl)amines and N-di(chloroethyl)amine hydrochlorides which were obtained are shown in Tables 1 and 2.

Preparation of 1,3- and 1,4-N-di(chloroethyl)aminocyclohexanecarboxylic acids. The ethyl esters of the N-di(chloroethyl)aminocyclohexanecarboxylic acids were heated with excess concentrated hydrochloric acid at 120-130° for 3 hours. The cooled solutions were treated with activated charcoal until decolorized and the hydrochloric acid was distilled off in a vacuum. Repeated additions of anhydrous ether and its distillation removed the residual hydrogen chloride. The product was dried in a vacuum desiccator over phosphorus pentoxide.

## SUMMARY

1) We have obtained N-di(chloroethyl)amine hydrochlorides of the alicyclic series.

2) We have described methods for obtaining some starting and intermediate substances.

## LITERATURE CITED

[1] C. E. Redemann, S. W. Chaikin and R. B. Fearing, J. Am. Chem. Soc. 70, 1648 (1948).

[2] J. Wislicenus and W. Hentzschel, Lieb. Ann. 275, 322 (1893); A. Müller and P. Bieler, Monatsh. 56. 391 (1930).

[3] G. Wendt, Ber. 75, 425 (1942); R. K. Patel and O. Gisvold, J. Am. Pharm. Assoc. 42, 321 (1953); A. Skita and W. Berendt, Ber. 52, 1519 (1919); A. Skita, R. Rössler, Ber. 72, 461 (1939).

[4] J. Wislicenus and W. Hentzschel, Lieb. Ann. 275, 322 (1893); E. D. Venus-Danilova, Zh. O. Kh. 6, 917 (1936); M. Godchot and F. Taboury, Comptes rend 152, 881 (1911); G. Vavon, Comptes rend 155, 286 (1912); C. R. Noller and R. Adams, J. Am. Chem. Soc. 48, 1080 (1926); Ia. M. Slobodin, M. V. Blinova and N. I. Deviatova, Zh. O. Kh. 24, 1639 (1954)*; R. F. Nystrom, and W. G. Bronn, J. Am. Chem. Soc. 69, 1199 (1947); L. Palfray, Bull. Soc. Chim. 7, 430 (1940).

[5] C. R. Noller and R. Adams, J. Am. Chem. Soc. 48, 1080 (1926); N. Turkiewicz, Zbl. 1939, II, 629.

[6] V. Ipat'ev, Zh. R. Kh. O. 15, 491 (1908).

[7] V. Markovnikov, Zh. R. Kh. O. 25, 364 (1893).

[8] E. Mosettig and A. Burger, J. Am. Chem. Soc. 52, 3456, 11 (1930).

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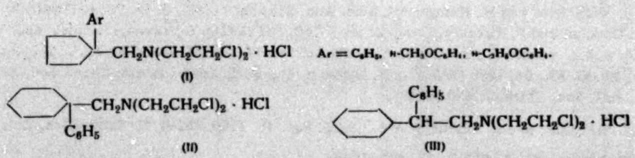
* Original Russian pagination. See C. B. Translation.

# N-DI(CHLOROETHYL)AMINES WITH ALICYCLIC AND AROMATIC RADICALS IN THE MOLECULE. II.

S. I. Sergievskaia, K. V. Levshina, A. I. Gavrilova
and A. K. Chizhov

The purpose of our study was to obtain N-di(chloroethyl)amines which contained in their molecule both aromatic and alicyclic radicals at the same time. The structure of these compounds is shown in the following scheme.


Ar
$CH_2N(CH_2CH_2Cl)_2 \cdot HCl$
$CH_2N(CH_2CH_2Cl)_2 \cdot HCl$
$C_6H_5$
$C_6H_5$
$CH—CH_2N(CH_2CH_2Cl)_2 \cdot HCl$

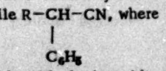
(I)

Ar = $C_6H_5$, n-$CH_3OC_6H_4$, n-$C_2H_5OC_6H_4$.

(II)

(III)

Compounds of types (I) and (II) are the arylated analogs of some N-di(chloroethyl)amines of the alicyclic series described in the preceding paper [1]. Compound (III) is distinguished from (I) and (II) by the fact that the aromatic radical in it is not a component part of the alicyclic radical.

To obtain these compounds we used as the starting substances the corresponding cyanides: for the synthesis of compounds of types (I) and (II), nitriles of the structure ArR−CN, for compound (III), the nitrile  $R-\underset{C_6H_5}{\underset{|}{CH}}-CN$, where R is the alicyclic radical. All these nitriles are easily obtained by condensing benzyl cyanide with the bromides (1,4-dibromobutane, 1,5-dibromopentane, and bromocyclohexane) in the presence of sodium amide. Among the nitriles which we thus obtained, only 1-(p-ethoxyphenyl)-1-cyanocyclopentane has not been described in the literature.

Reduction of the nitriles to the primary amines was carried out either by catalytic hydrogenation in the presence of Raney nickel, or with lithium aluminum hydride. Transformation of the amine to its N-di(hydroxyethyl) derivative and from the latter to the corresponding N-di(chloroethyl)amine was carried out by the method described in our previous paper [1].

Difficulty was encountered in the purification of the N-di(chloroethyl)amine hydrochlorides which contained the cyclohexyl radical: 1-(phenylcyclohexyl)-1-methyl-N-di(chloroethyl)amine hydrochloride was unstable and one atom of chlorine in it was quickly replaced by a hydroxyl group; therefore in the choice of solvents and in recrystallization a number of precautions had to be observed. It was also difficult to purify (β-phenyl-β-cyclohexyl)-ethyl-N-di(chloroethyl)-amine hydrochloride.

According to the preliminary results of the biological study, the introduction of the phenyl group in the molecule in these cases does not have a favorable effect on the anti-cancer activity of the compounds.

## EXPERIMENTAL

1-(p-Ethoxyphenyl)-1-cyanocyclopentane $C_5H_8(C_6H_4OC_2H_5)CN$. To 10 g of sodium amide in 100 ml of anhydrous toluene was gradually added 18.15 g of p-ethoxybenzyl cyanide in 65 ml of anhydrous toluene. The reaction mixture was heated on the boiling water bath until evolution of ammonia stopped, and then 24.4 g of 1,4-dibromobutane was added at such a rate that the temperature did not rise above 50°, after which the mixture was heated for 15 hours. After the mixture had cooled it was decomposed with 50 ml of water, the toluene layer was separated, the water was repeatedly extracted with toluene, and the toluene solutions were combined. After the toluene solution had been dried the toluene was distilled off and the residue distilled in a vacuum. B.p. 135-140° (0.3-0.4 mm).

Found %: N 6.47. $C_{14}H_{17}ON$. Calculated %: N 6.5.

In an analogous manner the previously described compounds were obtained: 1-(phenyl)-1-cyanocyclopentane [2], 1-(p-methoxyphenyl)-1-cyanocyclopentane [3], 1-(phenyl)-1-cyanocyclohexane [4], and the nitrile of phenylcyclohexyl acetic acid [5].

1-Phenyl-1-aminomethylcyclopentane $C_6H_5-C_5H_8-CH_2NH_2$. 50 g of 1-phenyl-1-cyanocyclopentane in solution in 200 ml of anhydrous methanol previously saturated with ammonia was hydrogenated in the presence of a skeletal nickel catalyst at 110-120° for 3.5 hours at an initial hydrogen pressure of 100 atm. After the catalyst had been removed and the solvent distilled, the residue was distilled in a vacuum. We collected the fraction with b.p. 129-130° (7 mm). Yield 43.44 g (85%). The substance was strongly basic and in air absorbed carbon dioxide.

The hydrochloride was obtained by the action of an ether solution of hydrogen chloride on an ether solution of the amine. White, crystalline substance. After recrystallization from anhydrous ethyl acetate it melted at 223-224°.

Found %: Cl 17.85, 17.72; N 7.07, 6.92. $C_{12}H_{15}NH_2 \cdot HCl$. Calculated %: Cl 17.9; N 7.1.

1-(p-Methoxyphenyl)- and 1-(p-ethoxyphenyl)-aminomethylcyclopentanes. To 0.47 mole of $LiAlH_4$ in 50 ml of anhydrous ether was added with stirring 0.027 mole of 1-(p-alkoxyphenyl)-1-cyanocyclopentane in 50 ml of anhydrous ether at such a speed that the reaction mass boiled weakly. After the addition of all the nitrile, the reaction mass was heated for 1 hour at the temperature of boiling ether. Then a small amount of water was carefully added to decompose the excess $LiAlH_4$ and 60 ml of 20% sodium hydroxide solution was added. The ether layer was separated and the water was extracted by ether; the combined ether solutions were dried over potassium hydroxide. The ether was distilled off and the residue vacuum distilled. The yield of 1-(p-alkoxyphenyl)-1-aminomethylcyclopentane was 90-95%.

The hydrochlorides of these amines were obtained by the action of an ether solution of hydrogen chloride on an ether solution of the amine. B.p. of 1-(p-methoxyphenyl)-1-aminomethylcyclopentane was 125-130° (3 mm). Its hydrochloride after recrystallization from anhydrous ethyl acetate melted at 174-175°.

Found %: C 64.26; H 8.11; Cl 14.7. $C_{13}H_{19}ON \cdot HCl$. Calculated %: C 64.60; H 8.30; Cl 15.01.

The boiling point of the fraction which contained chiefly 1-(p-ethoxyphenyl)-1-aminomethylcyclopentane was 115-130° (2 mm). Its hydrochloride melted after recrystallization from anhydrous ethyl acetate at 142-143°.

Found %: C 65.80; H 8.89; N 5.58; Cl 13.97. $C_{14}H_{21}ON \cdot HCl$. Calculated %: C 65.90; H 8.67; N 5.50; Cl 13.90.

1-Phenyl-1-aminomethylcyclohexane. $(C_6H_5)C_6H_{10}CH_2NH_2$. To a mixture of 2.93 g of lithium aluminum hydride and 155 ml of anhydrous ether was added dropwise a solution of 8.58 g of 1-phenyl-1-cyanocyclohexane in 20 ml of anhydrous ether. At the end of the reaction aqueous alkali was gradually added to the cooled reaction mixture. The further treatment was the same as previously described. We obtained 8.01 g (91.2%) of 1-phenyl-1-aminomethylcyclohexane.

B.p. 127.5-128° (3.5 mm), 129.5-131.1° (4 mm), $n^{20}D$ 1.5462.
Found %: C 82.74; H 10.10; N 7.57. $C_{13}H_{19}N$. Calculated %: C 82.50; H 10.10; N 7.40.

β-Phenyl-β-cyclohexylethylamine. $C_6H_5CH(C_6H_{11})CH_2NH_2$. 28.3 g of the nitrile of phenylcyclohexylacetic acid [5], 440 ml of 19.6% ammonia solution in methyl alcohol, and 17.5 g of skeletal nickel catalyst were placed in an autoclave and hydrogenated. (The initial hydrogen pressure at 20° was 77 atm.) The reaction mixture was heated to 120° and kept at this temperature for 3.5 hours. After the usual treatment of the reaction mixture and vacuum distillation of the methyl alcohol, the residue was vacuum distilled. We obtained a substance with b.p. 145° (5 mm); 122.5-123.5° (3 mm). The yield was nearly quantitative.

Found %: N 6.57. $C_{14}H_{21}N$. Calculated %: N 6.88.

N-di(hydroxyethyl)amines were obtained by heating the corresponding amine with ethylene oxide in a sealed tube at 130-140° for 3-6 hours. After 2 vacuum distillations they were used for the following reaction.

We obtained the following compounds.

1. (Phenylcyclopentyl)-methyl-N-di(hydroxyethyl)amine

$$(C_6H_5C_5H_8)CH_2N(CH_2CH_2OH)_2,$$

b.p. 224-227° (8 mm). Yield 93.5%.

2. (p-Methoxyphenylcyclopentyl)methyl-N-di(hydroxyethyl)amine, b.p. 195-210° (3 mm). Yield 80.4%.

3. (p-Ethoxyphenylcyclopentyl)methyl-N-di(hydroxyethyl)amine, b.p. 195-200° (3 mm). Yield 68.2%.

Found %: C 69.80; H 9.29; N 4.44. $C_{18}H_{29}O_3N$. Calculated %: C 70.04; H 9.45; N 4.56.

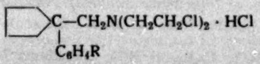
4. (Phenylcyclohexyl)methyl-N-di(hydroxyethyl)amine, b.p. 161.5-162° (1 mm). Yield 89.7%. $n^{20}_D$ 1.5443.

Found %: C 73.84; H 9.57; N 5.17. $C_{17}H_{27}O_2N$. Calculated %: C 73.60; H 9.81; N 5.06.

5. (β-Phenyl-β-cyclohexyl)ethyl-N-di(hydroxyethyl)amine, b.p. 192-195° (2.5 mm), $n^{20}D$ 1.5330.

Found %: C 74.08. H 10.08. $C_{18}H_{29}O_2N$. Calculated %: C 74.08; H 10.03.

N-di(chloroethyl)amines. a) N-di(chloroethyl)amines which contain the cyclopentyl radical were obtained from the corresponding N-di(hydroxyethyl)amines by the action of thionyl chloride on them. The reaction was carried out in chloroform solution at room temperature and the amines were obtained as their hydrochlorides. In most cases these were recrystallized from ethyl acetate; in the case of (p-methoxyphenylcyclopentyl)methyl-N-di(chloroethyl)amine hydrochloride, the substance was first dissolved in benzene and was precipitated from the benzene by anhydrous ether, and only after this purification was recrystallized from ethyl acetate. The N-di(chloroethyl)amine hydrochlorides of this series are shown in the Table.



$$C_5H_8{>}C(C_6H_4R){-}CH_2N(CH_2CH_2Cl)_2 \cdot HCl$$

| R | Melting point | Calculated (%) | | | | Found (%) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | C | H | N | Cl | C | H | N | Cl |
| H | 157—158° | 57.10 | 7.15 | 4.15 | 31.6 | 57.14 | 7.20 | 4.10 | 31.7 |
| $OCH_3$ | 128—129 | 55.80 | 7.10 | 3.82 | 29.1 | 55.90 | 7.37 | 3.77 | — |
| $OC_2H_5$ | 138—140 | 56.75 | 7.36 | 3.68 | 28.1 | 57.02 | 7.28 | 3.73 | — |

b) (1-Phenylcyclohexyl-1)methyl-N-di(chloroethyl) amine hydrochloride. The reaction of phenylcyclohexylmethyl-N-di(hydroxyethyl)amine (11.75 g) with thionyl chloride (7.22 ml) was carried out in a solution of anhydrous chloroform (35 ml) at 70-80°. After the chloroform and thionyl chloride had been distilled off in a vacuum, anhydrous benzene was added to the residue and it was distilled off in a vacuum; this operation was repeated several times. We obtained a crystalline precipitate (1.89 g) with m.p. 123-127°. After recrystallization from anhydrous benzene the substance melted at 123-125°. According to the analysis, the chlorine content of the substance was low, but the presence of a hydroxyl group was not detected.

Found %: Cl 28.57. $C_{17}H_{26}NCl_2 \cdot HCl$. Calculated %: Cl 30.38.

If the substance with m.p. 123-127° was recrystallized from anhydrous acetone or a mixture of alcohol and ether, we obtained a substance with m.p. 190-200°. The analysis of this substance showed that its composition was close to that of phenylcyclohexylmethyl-N-(hydroxyethyl) (chloroethyl)amine hydrochloride.

*(β-Phenyl-β-cyclohexyl)ethyl-N-di(chloroethyl)amine.* A mixture of 6.93 g of (β-phenyl-β-cyclohexyl) ethyl-N-di(hydroxyethyl)amine, 32 ml of chloroform, and 51.74 g of thionyl chloride was heated at 70° for 3 hours. Further treatment was the same as in the previous experiment. The resulting colored oil was treated with an excess of 50% solution of potash and the oil which formed was extracted with ether. After distilling off the ether we collected a substance with b.p. 168-179° (0.15 mm).

Found %: C 65.61, 65.38; H 8.13, 8.00; Cl 21.57. $C_{18}H_{27}NCl_2$. Calculated %: C 65.82; H 8.29; Cl 21.60.

The hydrochloride was obtained by the action of an ether solution of hydrogen chloride on the above base. It was purified by careful washing with anhydrous ether. We did not obtain the melting point since the substance decomposed when it was heated; it was easily soluble in water.

Found %: C 59.52; H 8.21. $C_{18}H_{27}NCl_2 \cdot HCl$. Calculated % C 59.30; H 7.73.

## SUMMARY

1. We have synthesized N-di(chloroethyl)amines which have not been described in the literature and also some other compounds of the cyclopentane and cyclohexanes series.

## LITERATURE CITED

[1] S. I. Sergievskaia, K. V. Levshina, A. K. Chizhov, A. I. Gavrilova and A. I. Kravchenko, Zh. O. Kh. 28, 1839 (1958).*

[2] K. V. Levshina and S. I. Sergievskaia, Zh. O. Kh. 22, 2191 (1952).*

[3] Ito Takeo, C. A. 48, 3999 (1954).

[4] R. E. Lyle and G. G. Lyle, J. Am. Chem. Soc. 74, 4059 (1952).

[5] E. D. Venus-Danilova and A. I. Bol'shukhin, Zh. O. Kh. 7, 2823 (1937).

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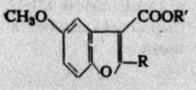
# THE ALKYLATION OF SUBSTITUTED 5-HYDROXYBENZOFURANS; SYNTHESIS OF NEW PLANT GROWTH STIMULANTS

A. N. Grinev, N. K. Venevtseva and A. P. Terent'ev

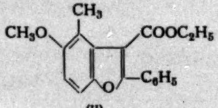
We have succeeded in working out a method of synthesis of substituted 5-hydroxybenzofurans by condensation of p-quinones with esters of β-ketoacids [1-5]. These investigations permitted getting a series of 5-hydroxybenzofuran derivatives. In order to show the structure of the resulting compounds, we have already in our work methylated some of them with dimethyl sulfate, and depending on the reaction conditions we have obtained either derivatives of 5-methoxybenzofuran-3-carboxylic acid [3, 5], or esters of the latter [6].

In the present work, by reaction of 5-hydroxybenzofurans with dimethyl sulfate in an alkaline medium in the presence of dioxane, we have obtained 2-phenyl-3-carbethoxy-5-methoxybenzofuran (I), 2-phenyl-3-carbethoxy-4-methyl-5-methoxybenzofuran (II), 2-phenyl-3-carbethoxy-5-methoxy-6-methylbenzofuran (III), 2-(p-nitrophenyl)-3-carbethoxy-5-methoxybenzofuran (IV), 2-methyl-3-carbethoxy-5-methoxy-6,7-dichlorobenzofuran (V), and 2-phenyl-3-carbethoxy-5-methoxy-6,7-dichlorobenzofuran (VI).

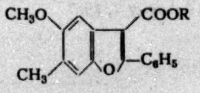
By hydrolysis of the esters (I), (III), (V) and (V) with alcoholic alkali we have obtained 2-phenyl-3-carboxy-5-methoxybenzofuran (VII), 2-phenyl-3-carboxy-5-methoxy-6-methylbenzofuran (VIII), 2-methyl-3-carboxy-5-methoxy-6,7-dichlorobenzofuran (IX), and 2-phenyl-3-carboxy-5-methoxy-6,7-dichlorobenzofuran (X). As a result of alkylation of the earlier synthesized hydroxyacids of the benzofuran chloroacetic acid series, we have obtained 2-methyl-3-carboxy-6,7-dichlorobenzofuran-5-hydroxyacetic acid (XI), and 2-phenyl-3-carboxy-6,7-dichlorobenzofuran-5-hydroxyacetic acid (XII)



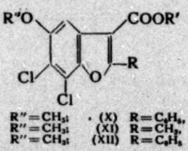
(I) $R = C_6H_5$, $R' = C_2H_5$;
(IV) $R = p\text{-}C_6H_4NO_2$, $R' = C_2H_5$
(VII) $R = C_6H_5$, $R' = H$;



(II)



(III) $R = C_2H_5$.
(VIII) $R = H$.



(V) $R = CH_3$, $R' = C_2H_5$, $R'' = CH_3$; (X) $R = C_6H_5$, $R' = H$, $R'' = CH_3$;
(VI) $R = C_6H_5$, $R' = C_2H_5$, $R'' = CH_3$; (XI) $R = CH_3$, $R' = H$, $R'' = CH_2COOH$;
(XI) $R = CH_3$, $R' = H$, $R'' = CH_3$; (XII) $R = C_6H_5$ $R' = H$, $R'' = CH_2COOH$.

The potassium salts of acids (VII-XII), tested in the Botanical Garden of Moscow State University by N. A. Bazilevskaia, were very effective stimulants for the growth of plants. The results of the biological study of these compounds will be published separately.

## EXPERIMENTAL

2-Phenyl-3-carbethoxy-5-methoxybenzofuran (I). 102 g of 2-phenyl-3-carbethoxy-5-hydroxybenzofuran with m.p. 154-155° [5] was dissolved in 200 ml of dioxane and the resulting solution was treated with 500 ml of 2 N sodium hydroxide (the solution became light green) and then with 100 ml of dimethyl sulfate. The reaction solution was shaken in a closed, thick walled vessel at room temperature for 35-40 minutes, diluted with 2-3 volumes of water, and well cooled. Crystals of 2-phenyl-3-carbethoxy-5-methoxybenzofuran (I) separated and were recrystallized from alcohol. Yield 95 g, m.p. 59-60°.

Found %: C 73.48, 73.52; H 5.60, 5.58. $C_{18}H_{16}O_4$. Calculated %: C 72.96; H 5.44.

2-Phenyl-3-carbethoxy -4-methyl-5-methoxybenzofuran (II). The reaction was carried out under the conditions of the preceding experiment. We took 28 g of 2-phenyl-3-carbethoxy-4-methyl-5-hydroxybenzofuran with m.p. 143-144° [2], 20 ml of dimethyl sulfate, 100 ml of 2 N sodium hydroxide, and 100 ml of dioxane. The yield of(II)was 28.8 g, m.p. 77-78° (from a mixture of alcohol and dioxane, 5 : 1)

Found %: C 74.15, 73.98; H 5.99, 6.09. $C_{19}H_{18}O_4$. Calculated %: C 73.53; H 5.85.

2-Phenyl-3-carbethoxy-5-methoxy-6-methylbenzofuran (III). For the experiment we took 85 g of 2-phenyl-3-carbethoxy-5-hydroxy-6-methylbenzofuran with m.p. 188-189° [2], 60 ml of dimethyl sulfate, 300 ml of 2 N sodium hydroxide, and 200 ml of dioxane. All the operations were carried out in the same way as in preparing (I). The yield of(III)was 90 g, m.p. 72-73° (from a mixture of alcohol and dioxane, 10 : 1).

Found %: C 73.64, 73.91; H 6.02, 6.03. $C_{19}H_{18}O_4$. Calculated %: C 73.53; H 5.85.

2-(p-Nitrophenyl)-3-carbethoxy-5-methoxybenzofuran (IV). For the experiment we took 3 g of 2-(p-nitrophenyl)-3-carbethoxy-5-hydroxybenzofuran with m.p. 208-210° [4], 2 ml of dimethyl sulfate, 10 ml of 2 N sodium hydroxide, and 15 ml of dioxane. All the operations were carried out as in the previous experiments. The yield of(IV)was 2.8 g, m.p. 167° (from a mixture of alcohol and dioxane, 1 : 2).

Found %: C 63.44, 63.48; H 4.66, 4.66. $C_{18}H_{15}O_6N$. Calculated %: C 63.34; H 4.43.

2-Methyl-3-carbethoxy-5-methoxy-6,7-dichlorobenzofuran (V). For the experiment we took 4.2 g of 2-methyl-3-carbethoxy-5-hydroxy-6,7-dichlorobenzofuran with m.p. 202.5° [1], 3 ml of dimethyl sulfate, 15 ml of 1 N sodium hydroxide and 28 ml of dioxane. All the operations were the same as before. Yield of (V), 4.1 g, m.p. 124-125° (from a mixture of ethyl alcohol and dioxane, 3 : 1).

Found %: C 51.95, 51.91; H 4.06, 4.12. $C_{13}H_{12}O_4Cl_2$. Calculated %: C 51.54; H 3.99.

2-Phenyl-3-carbethoxy-5-methoxy-6,7-dichlorobenzofuran (VI). For the experiment we took 4.2 g of 2-phenyl-3-carbethoxy-5-hydroxy-6,7-dichlorobenzofuran with m.p. 185-186° [1], 2.4 ml of dimethyl sulfate, 12.5 ml of 2 N sodium hydroxide, and 15 ml of dioxane. All the operations were carried out as in the previous experiments. Yield of(VI) 4 g, m.p. 149-150° (from a mixture of ethyl alcohol with dioxane, 1 : 1).

Found %: C 56.53, 56.68; H 3.99, 3.97. $C_{18}H_{14}O_4Cl_2$. Calculated %: C 56.46; H 3.86.

2-Phenyl-3-carboxy-5-methoxybenzofuran (VII ). 18 g of sodium hydroxide was dissolved in 200 ml of alcohol, and 45 g of ester(I)was added to the resulting solution. The reaction mixture was heated to boiling under reflux for 45 minutes, diluted with 200 ml of water, and filtered. Acidification of the filtrate with concentrated hydrochloric acid (to Congo) precipitated acid(VII). Yield 40 g, m.p. 176-177° (from acetic acid). A mixed melting point with an earlier preparation of compound(VII)[5] gave no depression.

2-Phenyl-3-carboxy-5-methoxy-6-methylbenzofuran (VIII). For the experiment we took 47 g of ester (III), 20 g of sodium hydroxide, and 170 ml of alcohol. All the operations were carried out as in the previous experiment. Yield of(VIII)40.5 g, m.p. 200-201° (from aqueous acetic acid.

Found %: C 72.63, 72.82; H 5.20, 5.27. $C_{17}H_{14}O_4$. Calculated %: C 72.33; H 5.00.

2-Methyl-3-carboxy-5-methoxy-6,7-dichlorobenzofuran (IX). For the experiment we took 3 g of ester (V), 1.2 g of sodium hydroxide, and 25 ml of alcohol. All operations were carried out as in the preparation of(VII). Yield of(IX)2.5 g, melts with decomposition at 319.5-321° (from acetic acid).

Found %: C 48.28, 48.49; H 3.07, 3.08. $C_{11}H_8O_4Cl_2$. Calculated %: C 48.02; H 2.97.

2-Phenyl-3-carboxy-5-methoxy-6,7-dichlorobenzofuran (X). For the experiment we took 2.8 g of ester (VI), 1.2 g of sodium hydroxide, and 25 ml of alcohol. All the operations were the same as before. Yield 2.4 g, m.p. 298-300° (from acetic acid).

Found %: C 56.63, 56.46; H 3.13, 3.15. $C_{16}H_{10}O_4Cl_2$. Calculated %: C 56.99; H 2.99.

2-Methyl-3-carboxy-6,7-dichlorobenzofuran-5-hydroxyacetic acid (XI). To a solution of 7.9 g of 2-methyl-3-carboxy-5-hydroxy-6,7-dichlorobenzofuran with m.p. 275-278° [1] in 14 ml of 40% sodium hydroxide solution was added 12 ml of 50% solution of monochloroacetic acid in water, and then 30 ml more of water. The reaction mixture was heated for 1 hour on the water bath. The sodium salt of acid(XI) was precipitated from the solution in the usual way. Yield of(XI) 8.5 g, m.p. above 260° (with decomposition).

Found %: C 42.62, 42.64 H 3.21, 3.37. $C_{12}H_{10}O_7Cl_2$. Calculated %: C 42.75; H 2.99.

2-Phenyl-3-carboxy-6,7-dichlorobenzofuran-5-hydroxyacetic acid (XII). To 3.5 g of 2-phenyl-3-carboxy-5-hydroxy-6,7-dichlorobenzofuran with m.p. 207° [1] was added 3.7 ml of 40% sodium hydroxide and ethyl alcohol to full solution of the precipitate. To the resulting solution was added 4 ml of 50% aqueous solution of monochloric acid. Further operations were carried out as in the previous experiment. Yield of(XI) 4 g (96.8), m.p. 288-289° (from acetic acid).

Found %: C 53.98, 54.05; H 2.89, 2.91. $C_{17}H_{10}O_6Cl_2$. Calculated %: C 53.56; H 2.64.

## SUMMARY

1. We have worked out a method for alkylating derivatives of 5-hydroxybenzofuran by the action of dimethyl sulfate on them.

2. By the reaction of 5-hydroxybenzofurans with chloroacetic acid we have obtained analogs of phenoxyacetic acid.

## LITERATURE CITED

[1] A. N. Grinev, Pan Bon Khvar, V. N. Frosin and A. P. Terent'ev, Zh. O. Kh. 26, 561 (1956).*

[2] A. N. Grinev, Pan Bon Khvar and A. P. Terent'ev, Vest. MGU, No. 2, 91 (1956).

[3] A. N. Grinev, Pan Bon Khvar, A. P. Terent'ev, Zh. O. Kh. 26, 2928 (1956).*

[4] A. N. Grinev, N. K. Venevtseva and A. P. Terent'ev, Zh. O. Kh. 26, 2933 (1956).*

[5] A. N. Grinev, Pan Bon Khvar and A. P. Terent'ev, Zh. O. Kh. 27, 821 (1957).*

[6] A. N. Grinev and A. P. Terent'ev, Zh. O. Kh. 28, 78 (1958).*

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# A NEW METHOD FOR OBTAINING SUBSTITUTED BENZOFURANS AND INDOLES FROM ESTERS OF BENZOFURAN- AND INDOLE-β-CARBOXYLIC ACIDS

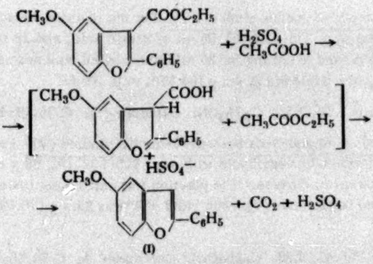
A. N. Grinev, I. A. Zaitsev, N. K. Venevtseva and A. P. Terent'ev

In a large number of cases esters of substituted benzofuran- and indole-β-carboxylic acids are more accessible than the benzofurans and indoles themselves. The carboxyl group in these compounds is held firmly enough, and its splitting off requires severe conditions which unavoidably lead to considerable loss of the substance [1, 2].

We have frequently had to carry out the removal of carboxyl groups in a number of substituted benzofuran-, benzodifuran-, and indole-β-carboxylic acids [3,6]. 2,6-Dimethyl- and 2,4,6-trimethylbenzo(1,2-b; 4,5-b')-difuran-3,7-dicarboxylic acids lose both carboxyls when heated with quinoline in the presence of copper oxide [3], but for the decarboxylation of benzofuran- and indole-β-carboxylic acids this process is not suitable. Some substituted benzofuran-β-carboxylic acids have been transformed into benzofurans in yields of about 50% by heating with calcium oxide [4, 5], but when other benzofuran acids of this type were decarboxylated by this method the yields of benzofurans were very small. We obtained 2-methyl-5-methoxyindole by heating 2-methyl-3-carboxy-5-methoxyindole to 140° in glycerine with a yield of 85% [6].

However, up to now we have not succeeded in carrying out the synthesis of N-alkyl or N-aryl substituted indoles with free β-positions by these or other processes.

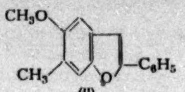
In the present work we give a number of examples of a successful method of splitting esters of benzofuran- and indole-β-carboxylic acids by heating them with equimolecular amounts of sulfuric or phosphoric acids in glacial acetic acid. The reaction goes by the following scheme

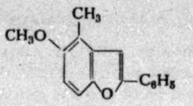


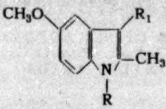
(I)

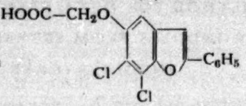
By splitting the corresponding esters with sulfuric acid in glacial acetic acid we obtained 2-phenyl-5-methoxybenzofuran (I), 2-phenyl-5-methoxy-6-methylbenzofuran (II), 2-phenyl-4-methyl-5-methoxybenzofuran (III), and 1,2-dimethyl-5-methoxyindole (IV), and by reaction with phosphoric acid, 1-phenyl-2-methyl-3-carbethoxy-5-methoxyindole (V) gave 1-phenyl-2-methyl-5-methoxyindole (VI).

2-Phenyl-3-carboxy-6,7-dichlorobenzofuran-5-hydroxyacetic acid was also split by sulfuric acid; it gave 2-phenyl-6,7-dichlorobenzofuran-5-hydroxyacetic acid (VII).


(II)


(III)


(IV) $R=CH_3$, $R_1=H$;
(V) $R=C_6H_5$, $R_1=COOC_2H_5$;
(VI) $R=C_6H_5$, $R_1=H$.


(VII)

## EXPERIMENTAL

1. Preparation of 2-phenyl-5-methoxybenzofuran (I). 5 g of 2-phenyl-3-carbethoxy-5-methoxybenzofuran with m.p. 59-60° [7] was dissolved in 25 ml of acetic acid and 5 ml of concentrated sulfuric acid was added to the resulting solution. The reaction mixture was heated for 1 hour at the boiling point and then cooled; the crystals which precipitated were separated and recrystallized from acetic acid. Yield of (I), 3 g (79.5%), m.p. 127°.

Found %: 80.36, 80.45; H 5.56, 5.49. $C_{15}H_{12}O_2$. Calculated %: C 80.33; H 5.39.

2. Preparation of 2-phenyl-5-methoxy-6-methylbenzofuran (II). For the reaction we took 9.2 g of 2-phenyl-3-carbethoxy-5-methoxy-6-methylbenzofuran with m.p. 72-73° [7], 46 ml of acetic acid, and 9.2 ml of concentrated sulfuric acid. Reaction and treatment were carried out as in experiment 1. Yield of (II), 6.5 g (91.5%), m.p. 150-150.5°.

Found %: C 80.65, 80.83; H 5.96, 6.08. $C_{16}H_{14}O_2$. Calculated %: C 80.64, H 5.92.

3. Preparation of 2-phenyl-4-methyl-5-methoxybenzofuran (III). For the reaction we used 13 g of 2-phenyl-3-carbethoxy-4-methyl-5-methoxybenzofuran with m.p. 77-78° [7], 65 ml of acetic acid, and 12 ml of concentrated sulfuric acid. Yield of (III), 9 g (90%), m.p. 79°.

Found %: C 80.90, 80.85; H 6.10, 6.18. $C_{16}H_{14}O_2$. Calculated %: C 80.64, H 5.92.

4. Preparation of 1,2-dimethyl-5-methoxyindole (IV). For the reaction we took 9.2 g of 1,2-dimethyl-3-carbethoxy-5-methoxyindole with m.p. 114-115° [8], 50 ml of acetic acid, and 10 ml of concentrated sulfuric acid. The reaction mixture was heated to boiling for 30 minutes, cooled, and neutralized with 2 N sodium hydroxide, and then steam distilled. Yield of (IV), 4.2 g (64.5%), m.p. 67-68°.

Found %: C 75.68, 75.86; H 7.70, 7.51. $C_{11}H_{13}ON$. Calculated %: C 75.40; H 7.48.

5. Preparation of 1-phenyl-2-methyl-3-carbethoxy-5-methoxyindole (V). For the reaction we used 32 g of 1-phenyl-2-methyl-3-carbethoxy-5-hydroxyindole with m.p. 205-206° [9], 28 g of dimethyl sulfate, 100 ml of 2 N sodium hydroxide, and 100 ml of dioxane. The reaction was carried out under the conditions for methylation of the 5-hydroxy substituted benzofurans [7]. The yield of (V) was 25.4 g (75.8%), m.p. 88-90° (from methanol).

Found %: C 74.22, 74.12; H 6.41, 6.39. $C_{19}H_{19}O_3N$. Calculated %: C 73.76; H 6.19.

6. Preparation of 1-phenyl-2-methyl-5-methoxyindole (VI). For the reaction we took 5.6 g of 1-phenyl-2-methyl-3-carbethoxy-5-methoxyindole, 20 ml of acetic acid, and 5 ml of concentrated phosphoric acid. The reaction mixture was heated to boiling for 1 hour, cooled, and neutralized for 2 N sodium hydroxide. The oil which precipitated crystallized when it stood for a week. The crystals were separated and recrystallized from benzine. Yield of (VI), 2.8 g (65.3%), m.p. 79-80°.

Found %: C 81.32, 81.25; H 6.17, 6.13. $C_{16}H_{15}ON$. Calculated %: C 80.98; H 6.37.

7. Preparation of 2-phenyl-6,7-dichlorobenzofuran-5-hydroxyacetic acid (VII). For the reaction we took 4.5 g of 2-phenyl-3-carboxy — 6,7-dichlorobenzofuran-5-hydroxyacetic acid with m.p. 288-289° [7], 45 ml of acetic acid, and 9 ml of concentrated sulfuric acid. The reaction mixture was boiled for 2 hours (to full solution of the precipitate). The resulting solution was diluted with water. The crystals which precipitated were separated, dried, and recrystallized from ethyl alcohol. Yield of (VII), 3.3 g (83.6%). A mixed melting point of the resulting preparation and 2-phenyl-3-carboxy-5-methoxy-6,7-dichlorobenzofuran [7] melted at 246-265°.

Found %: C 57.26, 57.12; H 3.22, 3.12. $C_{16}H_{10}O_4Cl_2$. Calculated %: C 56.99; H 2.99.

## SUMMARY

We have worked out a new method for preparing benzofurans and indoles from esters of benzofuran- and indole-β-carboxylic acids.

## LITERATURE CITED

[1] V. Titoff, H. Müller and T. Reichstein, Helv. Chim. Acta 20, 883 (1937).

[2] B. Dey, J. Chem. Soc. 107, 1651 (1915).

[3] A. P. Terent'ev, A. N. Grinev and Pan Bon Khvar, Zh. O. Kh. 24, 2050 (1954).*

[4] A. N. Grinev, Pan Bon Khvar and A. P. Terent'ev, Zh. O. Kh. 26, 2928 (1956).*

[5] A. N. Grinev, Pan Bon Khvar and A. P. Terent'ev, Zh. O. Kh. 27, 821 (1957).*

[6] A. N. Grinev, V. I. Shvedov and A. P. Terent'ev, Zh. O. Kh. 26, 1449 (1956).*

[7] A. N. Grinev, N. K. Venevtseva and A. P. Terent'ev, Zh. O. Kh. 28, 1851 (1958).*

[8] A. N. Grinev, I. A. Zaitsev, V. I. Shvedov and A. P. Terent'ev, Zh. O. Kh. 28, 446 (1958).*

[9] C. Nenitzescu, Bull. Soc. Chim. Romania 11, 37 (1929); C. A. 24, 110 (1930).

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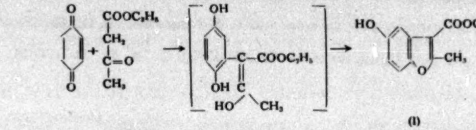
# STUDIES IN THE FIELD OF QUINONES

## XXIII. STUDIES OF THE CONDENSATION OF p-BENZOQUINONE AND 2,3-DICHLOROQUINONE WITH ACETOACETIC ESTER AND ITS ANALOGS

A. N. Grinev, N. K. Venevtseva and A. P. Terent'ev

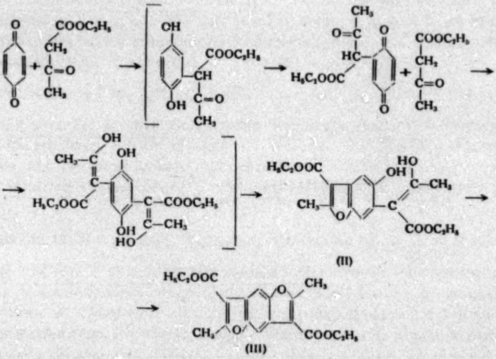
p-Benzoquinone, as has already been shown [1-5], reacts with acetoacetic and benzoylacetic esters, and if the reaction is carried out above 80°, depending on the concentration of p-benzoquinone in the reaction mixture, there is formed either mostly benzodifuran derivatives [1, 2, 4], or exclusively substituted benzofurans [3-5].

In the present work we have carried out the condensation of p-benzoquinone with acetoacetic ester at lower temperatures. These studies lead to results which differ from those obtained in the previous work. If the reaction between p-benzoquinone and acetoacetic ester proceeds at 80-85° and low concentrations of p-benzoquinone in the reaction mixture, the chief product (and with very small concentrations of p-benzoquinone, the only one) is benzofuran (I) [2, 3].



(I)

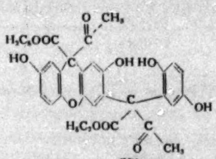
At 41-45° and also at low concentrations of p-benzoquinone in the reaction mixture there are formed [2-methyl-3-carbethoxy-5-hydroxybenzofuryl-(6)]-acetoacetic ester (II) and diethyl benzo [1,2-b; 4,5-b']-difuran-3,7-dicarboxylate (III).



(II)

(III)

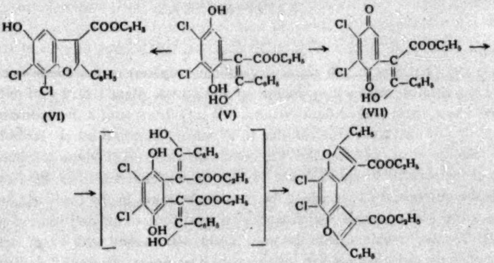
If the reaction is carried out at 38°, only the substituted benzofuran acetoacetic ester (II) is obtained. The latter is obtained without admixture of the benzodifuran derivative (III) when the concentration of zinc chloride in the reaction mixture is decreased. When a solution of the substituted benzofurylacetoacetic ester (II) in alcohol, acetic acid, or other solvents is boiled, it easily changes into the benzodifuran derivative (III). If the reaction is carried out at low temperatures, an increase in the relative concentration of p-benzoquinone in the reaction mixture produces in the reaction product along with the benzofuryl acetoacetic ester (II) a substance with m.p. 206.5-207°, for which the analysis and qualitative reactions indicate the structural formula of a dibenzopyran derivative (IV).



(VI)

In one of our studies [6], as the result of a careful separation of the reaction products from the reaction of 2,3-dichloroquinone with benzoylacetic ester, we isolated one of the hypothetical intermediate compounds, (3,4-dichloro-2,5-dihydroxyphenyl)-benzoylacetic ester (V). In the present paper we show that compound (V) is obtained in good yield if the condensation between 2,3-dichloroquinone and benzoylacetic ester is carried out at temperatures below 60°. The cyclization of the hydroquinone (V) into benzofuran (VI) proceess with definite speed only at 90°. If the temperature of the reaction mixture reaches 100°, the hydroquinone (V) cannot be isolated: it is completely cyclized into the benzofuran derivative (VI).

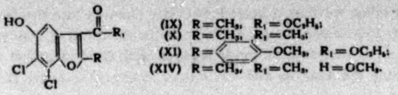
For confirmation of the reaction mechanism which we have assumed [2,6], (3,4-dichloro-2,5-dihydroxyphenyl)-benzoylacetic ester (V) was oxidized to the corresponding quinone (VII), and the latter was transformed by the action of benzoylacetic ester into the benzodifuran derivative (VIII), which was also isolated as a result of the reaction of 2,3-dichloroquinone with benzoylacetic ester [6].

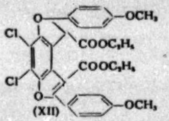


On the basis of these studies it is possible to conclude that the one or the other direction of the condensation of quinones with esters of $\beta$-ketoacids can easily be determined by a comparison of the yield of benzofuran and benzodifuran derivatives, and depends not only on the quinone concentration in the reaction mixture, but also to a considerable extent on the temperature at which the process is carried out. Besides these factors, the nature of the reagents, which react with the quinone also influence the yields of benzofuran and benzodifuran derivatives.

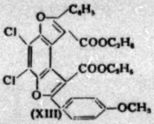
We carried out under the same conditions the condensation of 2,3-dichloroquinone with acetoacetic ester, acetylacetone, benzoylacetic ester, and p-methoxybenzoylacetic ester, and found that acetoacetic ester and acetylacetone react only to form the substituted benzofurans (IX) and (X). Condensation of 2,3-dichloroquinone with benzoylacetic and p-methoxybenzoylacetic esters leads to the formation of a mixture of derivatives of benzofuran

(VI, XI) and benzodifuran (VIII, XII); the yield of the benzodifuran derivative (XII) in the reaction of 2,3-dichloroquinone with p-methoxybenzoylacetic ester is greater than in the case of the benzoylacetic ester.


HO
O
C—R$_1$
R
O
Cl
Cl
(IX) R=CH$_3$, R$_1$=OC$_2$H$_5$;
(X) R=CH$_3$, R$_1$=CH$_3$;
(XI) R= —OCH$_3$, R$_1$=OC$_2$H$_5$;
(XIV) R=CH$_3$, R$_1$=CH$_3$, H=OCH$_3$.



(XII)



(XIII)

In explaining these results it is evidently necessary to consider both the nature of the β-ketoacid ester and the residue which acts as a substituent in the intermediate quinone (VII); the action of these two factors can be contradictory in character. Obviously the direction of the reaction is affected by the different solubilities in the reaction solvent of the intermediate hydroquinones* and differences in their reduction potentials. Since it was not possible in most experiments to isolate the intermediate hydroquinones and so establish their solubilities and reduction potentials, we followed another path: to study the effect of the nature of β-ketoacid ester which reacted with the quinone, we carried out a condensation of 2,3-dichloroquinone benzoylacetic ester (VII) with benzoylacetic ester and p-methoxybenzolacetic ester. We assumed that benzoylacetic and p-methoxybenzoylacetic esters would differ in activity and would react at different rates. Also, since the starting quinone rapidly formed a tar under the reaction conditions, we counted on obtaining the benzodifuran derivatives (VIII), (XIII), with different yields. If the yields of (VIII) and (XIII) differed greatly, then we could hope to increase the yield of benzodifuran derivative (XII) in the condensation of 2,3-dichloroquinone with p-methoxybenzoylacetic ester from the greater activity of the latter compared to benzoylacetic ester. However, the yield of benzodifuran derivatives (VIII) and (XIII) in the reaction of compound (VII) with benzoylacetic and p-methoxybenzoylacetic esters was about the same.

## EXPERIMENTAL

### Condensation of p-Benzoquinone with Actoacetic Ester

1. The reaction was carried out in an extractor (without a siphon) with a condenser protected by a calcium chloride tube. In the extractor thimble with a volume of 200 ml was placed 21.6 g of p-benzoquinone. The extractor was connected to a three-necked flask (volume 390 ml) fitted with a thermometer. In the flask was placed a solution of 27.3 g of anhydrous zinc chloride in 27 ml of anhydrous ethyl alcohol, 52.3 g of acetoacetic ester, and 120 ml of absolute ether, and the flask was heated on an air bath whose temperature was regulated so that the temperature of the solution in the flask was 44-45°; quinone was added to the flask by extraction during 11.5 hours. When all the quinone had been added the reaction mixture in the flask was kept at the same temperature for 1 hour more. The white crystals which separated were filtered off and washed with ether. Yield 5.2 g, m.p. 183-183.5°. The filtrate, combined with the wash liquid, was washed with water, and then from the solution 1.9 g more of crystals precipitated and had the same melting point. Diethyl 2,6-dimethylbenzo(1,2-b; 4,5-b')-difuran-3,7-dicarboxylate (III) melts, according to the literature, at 184°. A mixed melting point of substance (III) with pure substance (III) gave no depression. The total yield of diethyl 2,6-dimethylbenzo(1,2-b; 4,5-b')difuran-3,7-dicarboxylate (III) was 7.1 g (21.5%).**

The ether solution was dried over magnesium sulfate, the ether was distilled off in a vacuum, and the resulting thick oil remained overnight in a vacuum desiccator over phosphoric anhydride, after which it crystallized. The crystals were filtered and washed with methyl alcohol. Yield 11.2 g, (33.0%), m.p. 125-125.5° (from dichloroethane).

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*[3,4-Dichloro-2,5-dihydroxyphenyl]-benzoylacetic ester (V) for example, because of its poor solubility in the reaction solution, precipitates out.

**In all the experiments the yields are calculated on the starting quinone.

Found %: C 62.02, 61.78; H 5.90, 5.73. $C_{18}H_{20}O_7$. Calculated %: C 62.06; H 5.79.

The resulting white, crystalline substance was easily soluble in dichloroethane and dioxane, somewhat less so in ether. With heat it dissolved in alcohol, acetic acid, and all solvents which contained water; it was easily changed into the diethyl 2,6-dimethylbenzo(1,2-b; 4,5-b')difuran-3,7-dicarboxylate (III). With p-benzoquinone it did not form a quinhydrone, but with solutions of ferric chloride it gave a colored solution. From the analytical data and its chemical properties, the substance is [2-methyl-3-carbethoxy-5-hydroxybenzofuryl-(6)]acetoacetic ester (II).

2. For the reaction we took 21.6 g of p-benzoquinone, 52.3 g of acetoacetic ester, a solution of 13.6 g of anhydrous zinc chloride in 14 ml of anhydrous ethyl alcohol, and 120 ml of absolute ether. The reaction was carried out in the same way as in experiment 1, but the alcohol solution of zinc chloride was gradually added to the three necked flask from a dropping funnel. Before the reaction began, about 1/4 of the whole zinc chloride solution was added, and then it was added at the rate of 20-30 drops per hour. After 8 hours from the beginning of the reaction there was evident formation of quinhydrone, after which half the remaining zinc chloride solution was added, and over another hour, the rest. The addition of the zinc chloride solution took 9 hours. The reaction was run at 43-45°. p-Benzoquinone was extracted into the flask for 13.5 hours. After this the reaction mixture was kept at the same temperature for a further 1.5 hours. The resulting ether solution was treated as in experiment 1. Diethyl 2,6-dimethyl-benzo(1,2-b; 4,5-b')difuran-3,7-dicarboxylate (III) was not obtained. The yield of [2-methyl-3-carbethoxy-5-hydroxybenzofuryl-(6)]acetoacetic ester (II) was 10.5 g (30.2%), m.p. 125-126°. A mixed melting point with ester (II) obtained in experiment 1 gave no depression.

3. For the experiment we took 10.8 g of p-benzoquinone, 15.4 g of acetoacetic ester, a solution of 13.6 g of anhydrous zinc chloride in 14 ml of anhydrous ethyl alcohol, and 120 ml of absolute ether. Reaction was carried out as in experiment 1. p-Benzoquinone was extracted for 12.5 hours at 38°. After the addition of all the quinone the reaction mixture was kept at the same temperature for 1.5 more hours. The resulting ether solution was treated as in experiment 1. The yield of [2-methyl-3-carbethoxy-5-hydroxybenzofuryl-(6)]acetoacetic ester (II) was 6.3 g (36.3%), m.p. 125°. A mixed melting point with ester (II) from experiment 1 gave no depression.

4. For the experiment we took 10.8 g of p-benzoquinone, 15.4 g of acetoacetic ester, a solution of 13.6 g of anhydrous zinc chloride in 14 ml of anhydrous ethyl alcohol, and 120 ml of anhydrous ether. The reaction was run as in experiment 1, but at 40-41°. p-Benzoquinone was extracted for 11 hours. After addition of all the p-benzoquinone, the reaction mixture was kept at the same temperature for a further 1.5 hours. The resulting solution was treated as in experiment 1. After the solution was dried over magnesium sulfate, white crystals precipitated. They were filtered off, washed with ether, freed by water from magnesium sulfate, and dried. Yield 2.9 g (20.6%), m.p. 206.5-207°.

Found %: C 63.65, 63.58; H 4.73, 4.72. $C_{30}H_{28}O_{11}$. Calculated %: C 63.86; H 4.99.

The compound was easily soluble in dichloroethane, benzene, methyl and ethyl alcohols; poorly soluble in benzine. With p-benzoquinone it formed with heat a quinhydrone, and gave a color reaction with ferric chloride. From the analytical data and chemical properties it was a dibenzopyran derivative (IV).

From the ether solution we obtained 2.5 g (14.4%) of [2-methyl-3-carbethoxy-5-hydroxybenzofuryl-(6)]acetoacetic ester (II) with m.p. 124.5-125°. A mixed melting point with (II) obtained in experiment 1 gave no depression.

### Condensation of 2,3-Dichloroquinone with Acetoacetic Ester

1. The reaction was carried out in a three-necked flask connected with a stirrer, thermometer, and reflux condenser protected by a calcium chloride tube. In the flask we placed a solution of 6.8 g of anhydrous zinc chloride in 7 ml of anhydrous ethyl alcohol and 19.5 g of acetoacetic ester; the solution was heated to 100° on the water bath and 8.9 g of 2,3-dichloroquinone was quickly added to it. The reaction mixture was heated for 40 minutes with stirring on the water bath. The resulting crystals of 2-methyl-3-carbethoxy-5-hydroxy-6,7-dichlorobenzofuran (IX) were washed with water to remove zinc chloride, then with methyl alcohol, and were dried. Yield 7.3 g (53.5%), m.p. 196-197°. After 2 recrystallizations from methyl alcohol, the m.p. was 201° [7].

2. For the experiment we took 8.9 g of 2,3-dichloroquinone, a solution of 6.8 g of anhydrous zinc chloride in 7 ml of anhydrous ethyl alcohol, and 7.2 g of acetoacetic ester. Reaction was carried out as in the previous experiment. The acetoacetic ester was added to the alcoholic zinc chloride solution and the 2,3-dichloroquinone

was added to the resulting solution over 20 minutes at 85-90°. The reaction mixture was kept at the same temperature for 30 minutes more. The resulting crystals of 2-methyl-3-carbethoxy-5-hydroxy-6,7-dichlorobenzofuran (IX) were washed with water and methyl alcohol. Yield 4.8 g (35.2%), m. p. 195-196°. After 2 recrystallizations from methyl alcohol the m.p. was 200-201°; according to the literature it is 202.5° [7].

### Condensation of 2,3-Dichloroquinone with Acetylacetone

For the experiment we took 8.9 g of 2,3-dichloroquinone, a solution of 6.8 g of anhydrous zinc chloride in 7 ml of anhydrous ethyl alcohol, and 5.2 g of acetylacetone. The reaction was carried out in a manner analogous to the condensation of 2,3-dichloroquinone with acetoacetic ester. The resulting crystals were washed with water, methyl alcohol, and ether. Yield of 2-methyl-3-acetyl-5-hydroxy-6,7-dichlorobenzofuran (X) 7.4 g (57.2%). They melted with decomposition at 260.5° (from dioxane). White crystals, easily soluble in dioxane, toluene, and dichloroethane.

Found %: C 50.75, 50.70; H 3.11, 3.16. $C_{11}H_8O_3Cl_2$. Calculated %: C 50.99; H 3.11.

Preparation of 2-methyl-3-acetyl-5-methoxy-6,7-dichlorobenzofuran (XIV). To 2.8 g of 2-methyl-3-acetyl-5-hydroxy-6,7-dichlorobenzofuran (X) was added 70 ml of dioxane and 11 ml of 2 N sodium hydroxide solution. The resulting phenolate solution was treated in small portions with 9.5 ml of dimethyl sulfate. The reaction mixture was shaken on a rocker for 2 hours. The 2-methyl-3-acetyl-5-methoxy-6,7-dichlorobenzofuran (XIV) which was formed dissolved almost completely. The solution was diluted with double its amount of water and the precipitate was filtered. Yield 2.8 g (95.0%), m.p. 188-189° (from dioxane). White needles, easily soluble in dichloroethane and dioxane, less so in methyl alcohol.

Found %: C 52.79, 52.98; H 3.81; 3.84. $C_{12}H_{10}O_3Cl_2$. Calculated %: C 52.77; H 3.69.

### Condensation of 2,3-Dichloroquinone with Benzoylacetic Ester

1. For the experiment we took 7.5 g of 2,3-dichloroquinone, a solution of 5.7 g of anhydrous zinc chloride in 6 ml of anhydrous ethyl alcohol, and 8.8 g of benzoylacetic ester. The reaction was carried out analogously to the condensation of 2,3-dichloroquinone with acetoacetic ester at 100° (expt. 1). The resulting crystals were washed with water and methyl alcohol. Yield of 2-phenyl-3-carbethoxy-5-hydroxy-6,7-dichlorobenzofuran (VI) 8.0 g (54.5%), m.p. 184-186°. According to the literature [7], m.p. 185.5-186°. The benzodifuran derivative (VIII) was not found in this case.

2. For the experiment we took 20 g of 2,3-dichloroquinone, a solution of 15.4 g of anhydrous zinc chloride in 16 ml of anhydrous ethyl alcohol, 26.5 g of benzoylacetic ester, and 55 ml of absolute ether. The reaction was run under the conditions for the condensation of p-benzoquinone with acetoacetic ester (expt. 1), but the 2,3-dichloroquinone was extracted 2.5 hours in the reaction vessel at 55-61°. After addition of all the quinone, the reaction mixture was heated for 2 hours more. The white crystals which precipitated were filtered, washed with ether and water, and dried. Yield 8.9 g (45.5%), m.p. 164.5-165° (from dichloroethane).

Found %: C 55.22, 55.17; H 3.85, 3.82. $C_{17}H_{14}O_5Cl_2$. Calculated %: C 55.34; H 3.80.

The resulting substance was easily soluble in dichloroethane, acetic acid, and methyl and ethyl alcohols. It formed a quinhydrone with p-benzoquinone and gave a color reaction with ferric chloride. From the analytical results and the chemical properties it was (3,4-dichloro-2,5-dihydroxyphenyl)-benzoylacetic ester (V).

3. For the experiment we took 8.9 g of 2,3-dichloroquinone, a solution of 6.8 g of anhydrous zinc chloride in 7 ml of anhydrous ethyl alcohol, and 10.6 g of benzoylacetic ester. The reaction was run analogously to the condensation of 2,3-dichloroquinone with acetoacetic ester, but at 55-63°. The precipitating crystals were washed with water and methyl alcohol. Yield 10.6 g, m.p. 160-162°. The substance was dissolved in 265 ml of ethyl alcohol. When the solution cooled, crystals precipitated (0.1 g, 0.77%) with m.p. 229° which corresponded to the m.p. of diethyl 7,8-dichloro-2,5-diphenylbenzo(1,2-b; 5,6-b')-difuran-3,4-dicarboxylate (VIII) [6]. (3,4-Dichloro-2,5-dihydroxyphenyl)-benzoylacetic ester (V) separated when the alcohol solution was evaporated. The yield of ester(V) was 10.5 g (57.0%), m.p. 164-164.5° (after recrystallization from dichloroethane).

Oxidation of (3,4-dichloro-2,5-dihydroxyphenyl)-benzoylacetic ester (V) to the quinone (VII). Silver oxide, precipitated from a solution of 10 g of silver nitrate in water by 20% sodium hydroxide, was washed on the filter, 12 times with water, 6 times with acetone, and 6 times with absolute ether and placed in a beaker under a layer of absolute ether. 5.2 g of (3,4-dichloro-2,5-dihydroxyphenyl)-benzoylacetic ester (V) was dissolved in 410 ml of absolute ether and to the resulting solution was added 20 g of anhydrous magnesium sulfate and the prepared silver oxide. The reaction mixture was shaken for 10 minutes. The solution was separated from the precipitate and the ether distilled from it in a vacuum at room temperature. The resulting yellow crystals of the quinone (VII) were washed with a little ether. Yield 3.1 g (58.4%), m.p. 102-103°. After recrystallization from ether, m. p. 103.5-104°.

Found %: C 55.92, 55.71; H 3.39, 3.51. $C_{17}H_{12}O_5Cl_2$. Calculated %: C 55.60; H 3.29.

The resulting substance gave a quinhydrone with hydroquinone and a color reaction with ferric chloride.

### Condensation of the Quinone (VII) with Benzoylacetic Ester

In a test tube closed by a glass tube with a Bunsen valve was placed a solution of 0.4 g of anhydrous zinc chloride in 0.4 g of anhydrous ethyl alcohol, 0.67 g of benzoyl acetic ester, and 1 g of quinone (VII). The reaction mixture was heated for 1 hour on a boiling water bath. The resulting crystals were washed free of zinc chloride with water and then with methyl alcohol and ether. Yield 0.5 g (35.4%). After recrystallization from a mixture of dioxane and ethyl alcohol, m.p. 227°. A mixed melting point with pure diethyl 7,8-dichloro-2,5-diphenyl-benzo-(1,2-b; 5,6-b')-difuran-3,4-dicarboxylate (VIII) [6] gave no depression.

### Condensation of 2,3-Dichloroquinone with p-Methoxybenzoylacetic Ester

1. For the experiment we took 7.7 g of 2,3-dichloroquinone, a solution of 5.9 g of anhydrous zinc chloride, and 6 ml of anhydrous ethyl alcohol and 10.6 g of p-methoxybenzoylacetic ester [8]. The reaction was carried out under the conditions of condensation of 2,3-dichloroquinone with acetoacetic ester at 100° (experiment 1). The resulting crystals were washed with water and methyl alcohol, placed in an extractor thimble, and extracted with 3700 ml of ether. After removal of the ether we obtained 9.6 g (58%) of a substance with m.p. 175-176°. The pure substance melted at 183.5-184° (from ethyl alcohol).

Found %: C 56.97, 57.18; H 3.97, 3.81. $C_{18}H_{14}O_5Cl_2$. Calculated %: C 56.70; H 3.70.

According to the analytical data, this substance is 2-(p-methoxyphenyl)-3-carbethoxy-5-hydroxy-6,7-dichlorobenzofuran (XI). It was easily soluble in dichloroethane, dioxane, and ethyl alcohol.

In the residue after extraction was found 1 g (7.9%) of a white substance with m.p. 248.5-249°. The pure substance melted at 257.75° (from aqueous dioxane).

Found %: C 62.10, 62.03; H 4.21, 4.11. $C_{30}H_{24}O_8Cl_2$. Calculated %: C 61.76; H 4.13.

According to the analytical data this substance is diethyl 7,8-dichloro-2,5-di-(p-methoxyphenyl)-benzo (1,2-b; 5,6-b')-difuran-3,4-dicarboxylate (XII).

2. For the experiment we took 8.9 g of 2,3-dichloroquinone, a solution of 6.8 g of anhydrous zinc chloride in 7 ml of anhydrous ethyl alcohol, and 12.2 g of p-methoxybenzoylacetic ester. The reaction was carried out under the conditions of the condensation of 2,3-dichloroquinone with benzoylacetic ester at 85-90° [6]. The resulting crystals were washed with water and methyl alcohol, and extracted with 420 ml of ether. From the ether solution we obtained 6.8 g (35.7%) of 2-(p-methoxyphenyl)-3-carbethoxy-5-hydroxy-6,7-dichlorobenzofuran (XI), with m.p. 172.5-175°, m.p. 180° from dichloroethane. A test of the mixture with the preparation of (XI) obtained in the previous experiment gave no depression of the melting point.

After extraction there remained 2.6 g (17.8%) of diethyl 2,5-di(p-methoxyphenyl)-benzo-(1,2-b; 5,6-b')-difuran-3,4-dicarboxylate (XII) with m.p. 255-256°. A mixed melting point with preparation (XII) from the previous experiment gave no depression.

### Condensation of Quinone (VII) with p-Methoxybenzoylacetic Ester

For the experiment we took 1 g of quinone (VII), a solution of 0.75 g of anhydrous zinc chloride in 0.8 ml of anhydrous ethyl alcohol, and 1.3 g of p-methoxybenzoylacetic ester. The reaction was carried out as in the condensation of quinone (VII) with benzoylacetic ester. The yield of diethyl 7,8-dichloro-2-phenyl-5-(p-methoxyphenyl)-benzo(1,2-b; 5,6-b')-difuran-3,4-dicarboxylate (XIII) was 0.5 g (33.5%), m.p. 216.5°. The pure substance melted at 218.5-219° (from dioxane).

Found %: C 63.25, 63.36; H 4.12, 4.25. $C_{29}H_{22}O_7Cl_2$. Calculated %: C 62.94; H 4.01.

## SUMMARY

In examples of the condensation of p-benzoquinone and 2,3-dichloroquinone with acetoacetic ester and its analogs we have shown that the result of this reaction depends on the concentration of quinone in the reaction mixture and also on the reaction temperature and the nature of the reagents which react with the quinone.

The course of the reactions (isolation of intermediate products and separation of the different steps in the process) confirms our earlier assumption as to the mechanism of the reaction.

## LITERATURE CITED

[1] A.P. Terent'ev, A. N. Grinev and Pan Bon Khvar, Zh. O. Kh. 24, 2050 (1954).*

[2] A. N. Grinev, Pan Bon Khvar and A. P. Terent'ev, Zh. O. Kh. 26, 2928 (1956).*

[3] A. N. Grinev, Pan Bon Khvar and A. P. Terent'ev, Zh. O. Kh. 27, 1087 (1957).

[4] A. N. Grinev, Pan Bon Khvar and A. P. Terent'ev, Vest. MGU 2, 91 (1956).

[5] A. N. Grinev, Pan Bon Khvar and A. P. Terent'ev, Zh. O. Kh. 27, 821 (1957).*

[6] A. N. Grinev, N. K. Venevtseva and A. P. Terent'ev, Zh. O. Kh. 27, 1090 (1957).*

[7] A. N. Grinev, Pan Bon Khvar, V. N. Frosin and A. P. Terent'ev, Zh. O. Kh. 26, 561 (1956).*

[8] M. Wahl and C. Selbezweig, Bull. Soc. Chim. (4), 11, 27 (1911).

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# THE REACTION OF KETENE WITH NITROGEN-CONTAINING BASES

## VII. CHLOROACETYLATION OF PRIMARY AMINES

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The exceptional mobility of the chlorine atom in compounds of the type $RNHCOCH_2Cl$, $RNHCOCHCl_2$, and $RNHCOCCl_3$ has opened wide synthetic possibilities which were used in different fields of organic chemistry. Thus, for example, Stollé [1] and others have shown that chloroacetanilide is a good starting point for the synthesis of indigo dyes. Recently, α-chloroacetyl derivatives of amines have been widely used for obtaining physiologically active substances [2]. On the other hand, chloroacetanilide is itself interesting for medicine [3], since it is used for local anesthesia and as a substance to counteract the initiation of tuberculosis, angina, etc. This compound is also a rather strong insectofungicide.

At the present time, several methods are known for the synthesis of chloroacetanilide [4-9]. However, a distinguishing characteristic of these methods is the number of steps, the need for rare reagents, and the possibility of side reactions. From this point of view, the reaction of ketene with halogen substituted acids is promising; it proceeds through the formation of mixed anhydrides. The literature contains evidence of the chloroacetylating action of these anhydrides [10], but unfortunately, does not give a method of synthesis. Therefore we have worked out the synthetic part of the reaction of chloroacetylation from the beginning. The positive advantages of our method make it the simplest for obtaining chloroacetanilides.

## EXPERIMENTAL

To 10 g of monochloroacetic acid (m.p. 61°) placed in a three-necked flask fitted with a mechanical stirrer, reflux condenser, and glass inlet, was added ketene over 15-20 minutes.* After vacuum distillation we obtained a mixed anhydride of acetic and chloroacetic acids with b.p. 118-120° (110 mm) (12.7 g), which was cooled with a mixture of snow and salt and added with stirring to 7 g of aniline. The resulting precipitate remained for 10-20 minutes in the reaction vessel, then was recrystallized from water with active charcoal; m.p. 134°, yield 78%.

This operation could be carried out with the same yield in one step, without separating the pure anhydride. In this case, after passing ketene into the chloroacetic acid, the resulting liquid was added to the calculated amount of amine without cooling; then 1-2 ml of water was added. Immediately a voluminous precipitate of chloroacetyl derivative formed and was recrystallized from water.

The results of the work are given in the Table.

| Formula of chloroacetyl derivatives of the amine | Yield (in %) | Melting point | % Cl | |
|---|---|---|---|---|
| | | | Found | Calculated |
| $C_6H_5NHCOCH_2Cl$ | 78 | 134° | 20.53 | 20.93 |
| o-$CH_3C_6H_4NHCOCH_2Cl$ | 63 | 110—111 | 19.22 | 19.30 |
| m-$CH_3C_6H_4NHCOCH_2Cl$ | 72 | 141 | 19.15 | 19.30 |
| p-$CH_3C_6H_4NHCOCH_2Cl$ | 67 | 161 | 20.24 | 19.30 |
| p-J-$C_6H_4NHCOCH_2Cl$ | 58 | 189 | 12.07 | 11.99 |
| o-$CH_3OC_6H_4NHCOCH_2Cl$ | 61 | 49 | 17.52* | 17.60 |
| p-$CH_3OC_6H$·$MHCOCH_2Cl$ | 66 | 121.5 | 17.73* | 17.60 |

* The chlorine content was determined by the adsorption method.

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* Ketene was obtained by the pyrolysis of acetone at 700° (50 ml of acetone used).

## SUMMARY

We have given a new method for preparing chloroacetyl derivatives of amines by the action of chloroacetic acid and ketene on amines.

## LITERATURE CITED

[1] R. Stollé, J. pr. Ch. 128, 1 (1930); M. A. Wahe, V. Livovschi, Bull. Soc. Chim. 5, 653 (1938).

[2] F. Finkelstein, J. Am. Chem. Soc. 66, 407 (1944).

[3] J. Büchi, G. Launer and L. Ragaz, Helv. Chim. Acta 34, 278 (1951); Hikaru Ozawa, Kingo Enamoto, J. Pharm. Soc. Jap. 73, 719 (1953).

[4] D. Tommasi, Bull. Soc. Chim. (2), 19, 400 (1873); Ber. 7, 669 (1873); B. I. Meyer, Ber. 8, 1153 (1875); Piner, Fuch. Ber. 10, 1058 (1877); F. Reverdin, Helv. Chim. Acta 6, 87 (1923); M. A. Prokof'ev and Z. A. Rumiantseva, Uch. Zap. MGU 151, 349 (1951).

[5] C. O. Cech, Ber. 10, 1376 (1877).

[6] A. von Jonson, Zbl. 1906, II, 1694.

[7] M. F. Bodraux, Comptes rend 140, 1597 (1905); 141, 195 (1906).

[8] Beilst. 12, 243 (1929).

[9] C. A. Bischoff and P. Walden, Lieb. Ann. 279, 56, 62, 65 (1901).

[10] A. R. Emery and V. Gold, J. Chem. Soc. 1950, 1443.

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# STUDIES OF ORGANIC SULFUR COMPOUNDS

## I. THE SYNTHESIS OF ALKANESULFONYL FLUORIDES AND THEIR HALOGEN DERIVATIVES

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The class of aliphatic sulfonyl fluorides has been very little studied. The unsaturated sulfonyl fluorides have been studied still less and only vinylsulfonyl fluoride has been described [1]. Among the aliphatic sulfonyl fluorides which have been obtained there are substances with useful properties. Thus, methanesulfonyl fluoride is an effective insecticide [2], and the vinylsulfonyl fluoride which was mentioned copolymerizes with acrylonitrile to give a resin with high heat stability and plasticity [1].

In the present work we have carried out the synthesis of some alkanesulfonyl fluorides and their halogen derivatives (a number of which have not been described in the literature), in accordance with the general scheme:

$$RSO_2Cl \xrightarrow[HgF_2]{KF,\,ZnF_2} RSO_2F,$$

where $R = CH_3$, $n\text{-}C_3H_7$, $iso\text{-}C_3H_7$, $CH_2Cl$, $CH_2I$, $CH_2FCH_2$, $CH_3CHCl$, $CH_2ClCH_2$, $CH_2BrCH_2$, $CHCl_2CH_2$, $O_2NCH_2CH_2$.

Davis and Dick showed that the action of an aqueous solution of potassium fluoride on α-chloroethane-, cyclohexane-, and benzenesulfonylchloride gave the corresponding sulfonyl fluorides [3]. They carried out the reaction by heating the reacting substances with stirring; the precipitate of potassium chloride was dissolved in water; after ether extraction the dried extract was distilled. However, as these authors themselves showed, this method was not suitable for the synthesis of the first member of the series, methanesulfonyl fluoride, for the preparation of which they used another process (the action of zinc fluoride on methanesulfonyl chloride in a platinum vessel with heating).

We have found conditions by which methanesulfonyl fluoride can be prepared in good yield from methanesulfonyl chloride by the action of a saturated solution of potassium fluoride [4]. For this purpose the reacting substances are heated to boiling in a Favorskii flask and the methanesulfonyl fluoride which forms is distilled directly with steam. The methanesulfonyl fluoride which separates from the water layer contains almost no admixtures and comes over completely in the narrow temperature range (yield 65%).

In the same way we synthesized the undescribed n- and isopropanesulfonyl fluorides, and also iodomethanesulfonyl fluoride. Our experiments on obtaining this substance by the method of Davis and Dick showed that it could not be obtained in this way, and the first two substances formed along with contaminating impurities which were difficult to separate.

Thus, our method is simple and suitable for obtaining methane-, iodomethane-, n-propane- and isopropanesulfonyl fluorides.

We should say that the transformation of halogen substituted alkanesulfonyl chlorides (especially those substituted in the β-position) occurs with a sharply decreased yield of the corresponding sulfonyl fluorides because of competing processes [5] which in some cases become predominant. For example, β,β-dichloroethanesulfonyl fluoride cannot be obtained by the action of potassium fluoride in water solution, and this substance was obtained by the action of zinc fluoride on the starting sulfonyl chloride.* β-Chloroethanesulfonyl fluoride was isolated under the conditions of our reaction, but the yield was very low.

It is worthy of remark that the action of potassium fluoride, ammonium fluoride or zinc fluoride fails to convert trichloromethanesulfonyl chloride into trichloromethanesulfonyl fluoride; either the reaction does not occur at all, or there is deep destruction of the molecule with formation of carbon tetrachloride, hexachloroethane, and sulfur dioxide.

The increment of atomic refraction of fluorine in the sulfonyl fluorides which we have synthesized differs from the figure accepted for this value (0.997-1.08). In most cases the value for the atomic refraction of fluorine in the sulfonyl fluorides is close to 1.61, although we have found considerable variation on one side or the other depending on the structure and characteristics of the substituents in the hydrocarbon radical. Such a high value for the atomic refraction of fluorine has also been observed in other compounds which contain fluorine [6].

## EXPERIMENTAL

Methanesulfonyl fluoride (I). We placed in a Favorskii flask 30 g of methanesulfonyl chloride and 90.9 g of a 70% solution of potassium fluoride. The mixture was heated on a wire gauze until distillation of a two layer liquid stopped (89-90°). The distillate was separated, the organic layer was dried over calcium chloride, and distilled. Yield of (I) 18 g (65%).

B.p. 124-124.2°, $n^{20}D$ 1.3568, $d^{20}_4$ 1.3470, $MR_D$ 15.94, $AR_F$ 1.61.
Literature data for (I): b.p. 124.2° (754 mm), $n^{20}D$ 1.3596 [3].

n-Propanesulfonyl fluoride (II). n-Propane- and isopropanesulfonyl chlorides were separated by fractional distillation from the product of sulfochlorination of propane. 16.8 g of n-propanesulfonyl chloride (b.p. 76-78° at 13 mm, $n^{20}D$ 1.4536) was treated with 24 g of saturated potassium fluoride solution and the 90-94° fraction was collected. The organic layer after drying over calcium chloride came over completely in the range 148-150° (749 mm).

$n^{20}D$ 1.3865, $d^{20}_4$ 1.2003, $MR_D$ 24.71; calcd. 24.56; $AR_F$ 1.14.
Found %: F 15.2, 15.4. $C_3H_7O_2SF$. Calculated %: F 15.07.

Isopropanesulfonyl fluoride (III). From 50 g of isopropanesulfonyl chloride (b.p. 71.0-73° at 13 mm, $n^{20}D$ 1.4520) and 76 g of 70% potassium fluoride solution we obtained (III) (not containing chloride).

B.p. 144-146° (751 mm), $n^{20}D$ 1.3895, $d^{20}_4$ 1.1600, $MR_D$ 25.74; calcd. 24.56.
Found %: F 15.5, 15.6. $C_3H_7O_2SF$. Calculated %: F 15.07.

Chloromethanesulfonyl fluoride (IV). As the starting substance we used chloromethanesulfonyl chloride, obtained by oxidative chlorination of 1,3,5-trithiane, which was formed by the action of hydrogen sulfide on paraform in a hydrochloric acid medium [7]. 151 g of chloromethanesulfonyl chloride (b.p. 172-174°) was treated with 300 g of a solution of potassium chloride under the conditions of Davis and Dick. We obtained 59 g of (IV); yield 43.7%.**

B.p. 130-132°, $n^{20}D$ 1.4123, $d^{20}_4$ 1.5980, $MR_D$ 20.58; calcd. 20.64.
Literature data for (VI) [8]: b.p. 131.5-132°.

Iodomethanesulfonyl fluoride (V). 50 g of skiodan was treated with 44 g of phosphorus pentachloride with shaking. When the reaction was ended (the mixture no longer warmed spontaneously), the content of the flask was poured onto ice and the oil which precipitated was extracted with benzene; the extract was dried with calcium chloride and distilled. We obtained 46 g (91.2%) of iodomethanesulfonyl chloride.

B.p. 82-83° (2 mm), b.p. 93° (5 mm), $n^{20}D$ 1.4840, $d^{20}_4$ 2.4465, $MR_D$ 32.91; calc. 33.36.

21.5 g of iodomethanesulfonyl chloride was treated with 45 g of a saturated solution of potassium fluoride and substance (V) was obtained.

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* β,β-Dichloroethanesulfonyl chloride, described by Iakubovich and Zinov'ev [13], can be prepared, as Kochetkov showed, by combination of sulfuryl chloride and vinyl chloride in the presence of aluminum chloride [14].

** Under the conditions described for (I), the yield of chloromethanesulfonyl fluoride fell to 29.4%.

B.p. 64-64.5° (5 mm), $n^{20}D$ 1.5090, $d^{20}{}_4$ 2.3236; $MR_D$ 28.76; calcd. 28.12.
Found %: C 5.93, 5.98; H 1.26, 1.02; S 14.11 , 13.74; F 7.99, 8.27. $CH_2O_2SFI$. Calculated %: C 6.57; H 0.89; S 14.9; F 8.45.

*β-Fluoroethanesulfonyl fluoride (VI).* The starting β-fluoroethanesulfonyl chloride was obtained in 57% yield and identified by its constants [9]. From 15.5 g of β-fluoroethanesulfonyl chloride (b.p. 82-85° at 13 mm, $n^{20}D$ 1.4570) and 40 g of potassium fluoride we obtained 4.8 g of a substance with b.p. 118-120° at 757 mm ($n^{20}D$ 1.3845 [5]) and substance (VI).

B.p. 164-166° (757 mm), $n^{20}D$ 1.4150, $d^{20}{}_4$ 1.4157, $MR_D$ 23.06.
Found %: F 30.4, 30.6. $C_2H_4O_2SF_2$. Calculated %: F 29.09.

*α-Chloroethanesulfonyl fluoride (VII).* 16 g of α-chloroethanesulfonyl chloride was reacted with 36 g of a solution of potassium fluoride under the conditions of Davis and Dick. We obtained 1.5 g (10.5 ) of substance (VII).

B.p. 138.0-139° (760 mm), $n^{20}D$ 1.4080, $d^{20}{}_4$ 1.4420, $MR_D$ 25.05; calcd. 25.01.
Literature data for (VII)[3]: b.p. 138-139° (760 mm), $n^{20}D$ 1.4070.

*β-Chloroethanesulfonyl fluoride (VIII).* β-Chloroethanesulfonyl chloride was obtained according to the data of [10]. To 17.9 g of β-chloroethanesulfonyl chloride (b.p. 70-71° at 5 mm, $n^{20}D$ 1.4910) was added 45 ml of a saturated solution of potassium fluoride and the reaction was carried out as described for (I). The organic layer, dried over calcium chloride, was distilled and fractions were separated: 1st, 118-120° (747 mm), $n^{20}D$ 1.3850, 10.9 g; 2nd, 164-166° (757 mm), $n^{20}D$ 1.4258, 2.3 g; 3rd, 170-172° (758 mm), $n^{20}D$ 1.4337, 1.7 g. The 1st and 2nd fractions were not further studied; the 3rd was substance (VII).

B.p. 170-172° (758 mm), $n^{20}D$ 1.4337, $d^{20}{}_4$ 1.5007, $MR_D$ 25.41; calcd. 25.01.
Found %: Cl 24.6, 24.8; F 12.45, 12.74. $C_2H_4O_2SFCl$. Calculated %: Cl 24.21; F 12.95.

*β-Bromoethanesulfonyl fluoride (IX).* β-Bromoethanesulfonyl chloride was obtained by the reaction of 1,2-dibromoethane and sodium sulfite with later treatment of the thus formed β-bromoethanesulfonate by phosphorus pentachloride [11]. Substance (IX) was synthesized from 8 g of a saturated potassium fluoride solution and 3 g of β-bromoethanesulfonyl chloride.

B.p. 77° (5 mm), $n^{20}D$ 1.4870.
Found %: F 10.4, 10.4. $C_2H_4O_2SFBr$. Calculated %: F 9.95.

*β,β-Dichloroethanesulfonyl fluoride (X).* 20 g of β,β-dichloroethanesulfonyl chloride was heated 18 hours in a platinum flask with 20 g of zinc fluoride* to 100-160°; 4 more g of zinc fluoride was added and heating was continued for 6 hours to 165-170°. We obtained 4.5 g (25%) of substance (X).

B.p. 62-64° (5 mm), b.p. 74-76° (25 mm), $n^{20}D$ 1.4527, $d^{20}{}_4$ 1.6169, $MR_D$ 30.24; calcd. 29.88.
Found %: F 10.17, 10.20. $C_2H_3O_2SFCl_2$. Calculated %: F 10.49.

*β-Nitroethanesulfonyl fluoride (XI).* In a boiling solution of 48 g of potassium hydroxide in 68 g of water was passed sulfur dioxide to a weakly alkaline reaction (pH 9). The resulting solution of potassium bisulfite at 30° was treated dropwise with 52 g of β-nitroethylacetate. We obtained 45 g of the potassium salt of β-nitroethanesulfonic acid (yield 59%) which after careful drying was mixed with 68.5 g of phosphorus oxychloride and 62 g of phosphorus trichloride and was chlorinated with gaseous chlorine for 2 hours. The reaction mass was then filtered, the precipitate washed with phosphorus oxychloride, and the filtrate was distilled. After the phosphorus oxychloride was distilled off the residue was decomposed with water and the oil which precipitated was extracted with benzene. After the benzene had been distilled off the residue of β-nitroethanesulfonyl chloride** (1.6 g) was treated in the cold with mercuric fluoride (in portions). Reaction took place violently, with strong heating. The reaction mixture was extracted three times with ether, the ether extract was washed with 10% hydrochloric acid, and with water, dried over sodium sulfate, and distilled. We collected the fraction (XI) with b.p. 80-82° (2 mm), $n^{20}D$ 1.4352.

Found %: F 12.2, 11.9. $C_2H_4O_4NFS$. Calculated %: F 12.0.

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*The action of an aqueous solution of potassium fluoride did not give a pure preparation of substance (X).

**The preparation of β-nitroethanesulfonyl chloride was carried out by the method of Gold and Druner [12].

Action of zinc, antimony, and potassium fluorides on trichloromethanesulfonyl chloride. Equimolecular amounts of trichloromethanesulfonyl chloride and zinc fluoride were carefully heated in a platinum flask. The liquid which passed over completely below −10° was collected in a trap cooled to −78° and absorbed by a solution of sodium hydroxide. This substance was identified as sulfur dioxide. From the reaction mass was distilled a fraction (b.p. 74-78°, $n^{20}D$ 1.4614, $d^{20}_4$ 1.593) which was carbon tetrachloride. At 150° white crystals came over (m.p. 172-175°) which had a characteristic odor, were poorly soluble in ether, and after two sublimations melted at 182-184°; they were hexachloroethane. The action of antimony trichloride on trichloromethanesulfonyl chloride led to analogous products. A solution of potassium fluoride under the conditions of Davis and Dick had no action on trichloromethanesulfonyl chloride.

## SUMMARY

1. We have synthesized n-propane-, isopropane-, iodomethane-, β-fluoroethane-, β-chloroethane-, β-bromoethane-, β-nitroethane-, and β,β-dichloroethanesulfonyl fluorides, which have not been described in the literature.

2. We have shown that heating methane-, n-propane-, isopropane-, and iodomethanesulfonyl chlorides with a saturated solution of potassium fluoride with continuous steam distillation of the resulting sulfonyl fluorides is a satisfactory preparative method for the synthesis of these substances.

## LITERATURE CITED

[1] Am. patent 2653973 (1953); C. A. 48, 8813 (1954).

[2] G. Shrader, Usp. Khim. No. 6, 712 (1953).

[3] W. Davis and J. Dick, J. Chem. Soc. 1931, 2104; 1932, 483, 2042.

[4] L. Z. Soborovskii, B. M. Gladshtein and M. I. Kiseleva, Author's certificate No. 108713 (1955).*

[5] L. Z. Soborovskii, B. M. Gladshtein, M. I. Kiseleva and V. N. Chernetskii, Zh. O. Kh. 28, 1870 (1958).**

[6] A. Henne, C. Fox. J. Am. Chem. Soc. 76, 479 (1954).

[7] T. Johnson and J. Douglass, J. Am. Chem. Soc. 63, 1571 (1941).

[8] E. Gryszkiewicz-Trochimowski, Rec. trav. chim. 66, 413 (1947); C. A. 1948, 865.

[9] B. Saunders, G. Stacey and J. Wilding, J. Chem. Soc. 1949, 775.

[10] R. Hübner, Lieb. Ann. 223, 198 (1881).

[11] E. Landau, J. Am. Chem. Soc. 69, 1219 (1947).

[12] M. Gold and L. Druner, J. Org. ch. 16, 1511 (1951).

[13] A. Ia. Iakubovich and Iu. M. Zinov'ev, Zh. O. Kh. 17, 2028 (1947).

[14] N. K. Kochetkov, Zh. O. Kh. 23, 744 (1953).**

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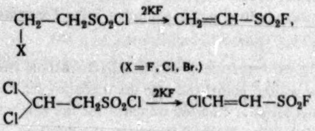
## STUDIES OF ORGANIC SULFUR COMPOUNDS

## II. THE SYNTHESIS OF ALKENESULFONYL FLUORIDES AND THEIR HALOGEN DERIVATIVES

L. Z. Soborovskii, B. M. Gladshtein, V. N. Chernetskii
and M. I. Kiseleva

In the previous communication we showed that potassium fluoride in water solution acted on some alkanesulfonyl chlorides with continuous steam distillation of the reaction products to give a satisfactory preparative method for the synthesis of some alkane- and haloalkanesulfonyl fluorides [1].

A study of the reaction of potassium fluoride with halogen substituted ethane sulfonyl chlorides showed that along with the replacement of chlorine by fluorine there occurred a process of dehydrohalogenation, as a result of which unsaturated sulfonylfluorides were formed.



$$CH_2X-CH_2SO_2Cl \xrightarrow{2KF} CH_2=CH-SO_2F,$$

(X = F, Cl, Br.)

$$Cl_2CH-CH_2SO_2Cl \xrightarrow{2KF} ClCH=CH-SO_2F$$

The ability of alkali fluorides to combine with hydrogen halides and thus give double salts has long been known. Earlier [2] the ability of potassium fluoride to split hydrogen chloride from acid chlorides and alkyl halides was demonstrated.

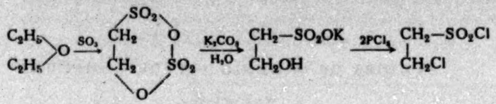
The property of potassium fluoride of splitting hydrogen halides from two adjacent hydrocarbon atoms permitted us to carry out a direct transformation from a halogen derivative of an alkanesulfonyl chloride to a sulfonyl fluoride of the unsaturated series in one step and with good yield. Up to now, only one example of this series has been described, vinylsulfonyl fluoride [3].

This reaction has been used for the synthesis of the unsaturated aliphatic sulfonyl fluorides and their halogen derivatives. The constants of the resulting substances are given in Table 1.

TABLE 1

| Substance | Boiling point | Pressure (mm) | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ found | $MR_D$ calc. | Melting point |
|---|---|---|---|---|---|---|---|
| $CH_2=CH-SO_2F$ | 118–120° | 747 | 1.3850 | 1.3329 | 19.37 | 19.58 | — |
| $ClCH=CH-SO_2F$ (low boiling) | 42.7–43.1 | 25 | 1.4170 | 1.5384 | 24.40 | 24.44 | −45.8° |
| $ClCH=CH-SO_2F$ (high boiling) | 45.0 | 25 | 1.4321 | 1.5247 | 24.58 | 24.44 | −22.2 |
| $ClCH=CHSO_2Cl$ | 50–52 | 3 | 1.5043 | 1.5858 | 30.09 | 29.69 | — |

The starting substances for the synthesis of sulfonyl fluorides of the unsaturated type and their halogen derivatives, as was said above, were the haloalkanesulfonyl chlorides. Thus, β-chloroethanesulfonyl chloride, for whose synthesis no satisfactory method is described in the literature, was obtained by the method of Hübner [4].



It should be said that when β-chloroethanesulfonyl chloride was obtained by this method, the yields were low. The use of an improved method did not affect the yield [5].

A very satisfactory process for preparing β,β-dichloroethanesulfonyl chloride is that described by Kochetkov by direct combination of sulfuryl chloride with vinyl chloride in the presence of anhydrous aluminum chloride [6].

The resulting β-chloro- and β,β-dichloroethanesulfonyl chlorides were transformed into vinyl- and β-chlorovinylsulfonyl chlorides by the action of potassium fluoride. An analogous procedure was applied to the action of potassium fluoride on β-fluoro- and β-bromoethanesulfonyl chlorides, whose preparation was described earlier [1].

We isolated two fractions with similar boiling points from β-chlorovinylsulfonyl fluoride, which were stereoisomers (Table 1). In many cases in the ethylene series of hydrocarbons the isomers with the lower values for boiling point and constants have the trans configuration, and the isomers with the higher boiling points and higher constants have the cis configuration. However, the reverse relationship is often found. Neither these nor any other regularities exist between boiling points and other basic constants for the isolated fractions of β-chlorovinylsulfonyl fluorides.

Examples are described in the literature of ethylene hydrocarbons (with established or unknown configurations), the regularities of whose boiling points and also the tendency for the constants to change is similar to those found for the β-chlorovinyl sulfonyl fluoride isomers: for the low boiling isomer the refractive index is lower and the specific gravity is higher. Table 2 illustrates these values.

Thus, substances with freezing points of −45.0 and −22.2° (Table 1) on the basis of elementary analysis, constants, and molecular refraction can be ascribed the structures of cis and trans β-chlorovinylsulfonyl fluoride.

TABLE 2

| Substance | Boiling point | $n^t_D$ | $d^{20}_4$ |
|---|---|---|---|
| 3,5,5-Trimethyl-2-heptene (low boiling) [7] | 160.3° | 1.4367 (25°) | 0.7850 |
| 3,5,5-Trimethyl-2-heptene (high boiling) [8] | 162.1 | 1.4388 (25 ) | 0.7756 |
| Cis-1-phenyl-1-propene [9] | 64.5 (20 mm) | 1.5400 (20 ) | 0.9107 |
| Trans-1-phenyl-1-propene [9] | 73.5 (20 mm) | 1.5473 (20 ) | 0.9019 |

## EXPERIMENTAL

Vinylsulfonyl fluoride (I). a) To 35.8 g of β-chloroethanesulfonyl chloride [4] (b.p. 70-71° (5 mm) $n^{20}D$ 1.4910) was added 90 ml of a saturated solution of potassium fluoride, the mixture was heated in a Favorskii flask; it was gradually brought to boiling, and the distillate was collected in the range 92-99°. The organic layer of the distillate was dried over calcium chloride and gave 21.8 g of (I) (yield 45.3%).

B.p. 118-120° (747 mm), $n^{20}D$ 1.3850, $d^{20}_4$ 1.3329, $MR_D$ 19.37.
Found %: C 22.75, 22.76; H 3.08, 2.80; S 28.11; F 16.4, 16.6. $C_2H_3O_2SF$. Calculated %: C 22.8; H 2.73; S 29.0; F 17.2.
Literature data for (I) [3]: b.p. 44-46° (50 mm).

(I) decolorized acidified potassium permanganate solution, but did not react particularly with a solution of bromine in carbon tetrachloride.

Besides this, we isolated by distillation 3.5 g of a fraction with b.p. 170-172° (758 mm), identified as β-chloroethanesulfonyl fluoride, which was described earlier [1].

b) Under these conditions 17.2 g of vinylsulfonyl chloride (b.p. 68° (20 mm)) and 49 g of potassium fluoride gave 6 g of (I) (yield 40%).

c) 15.5 g of β-fluoroethanesulfonyl chloride (obtained according to [10]) and 40 g of potassium fluoride under analogous conditions gave 4.8 g of (I) ($n^{20}D$ 1.3845), and β-bromoethanesulfonyl chloride [11] gave 43% conversion to (I).

β-Chlorovinylsulfonyl chloride (II). To 50 g of β,β-dichloroethanesulfonyl chloride [6] in 100 ml of absolute ether was added over 3 hours 25 g of triethylamine in 60 ml of absolute ether, dropwise with energetic stirring and cooling to −45 to −65°. The mixture was then brought to room temperature, 50 ml of 1% sulfuric acid was added, it was cooled to 0°, the ether layer was washed once more with 1% sulfuric acid, then water and a 20% solution of sodium chloride, then dried over sodium sulfate, and distilled. We obtained (II) (12 g, that is, 30%) (in the form of a mixture of cis and trans forms) with the following constants:

B.p. 50-52° (3 mm), $n^{20}D$ 1.5043, $d^{20}_4$ 1.5858, $MR_D$ 30.09.
Found %: C 15.71, 15.72; H 1.43, 1.55; Cl 40.96, 40.86. $C_2H_2O_2SCl_2$. Calculated %: C 14.91; H 1.24; Cl 42.65.

β-Chlorovinylsulfonyl fluoride (III). 100 g of β,β-dichloroethanesulfonyl chloride was treated with 150 g of saturated solution of potassium fluoride as for (I); we obtained 30.7 g (40.1%) of a fraction with b.p. 34-49° (25 mm). The accumulation from several experiments of this fraction (200 g in all) was vacuum distilled in a rectifying column. The isolated fractions were: 1, b.p. 42.7-43.1° (25 mm), and 2, b.p. 45° (25 mm).

Properties of fraction 1.

M.p. −45°, $n^{20}D$ 1.4170, $d^{20}_4$ 1.5384, $MR_D$ 24.40.
Found %: C 16.64, 16.53; H 1.96, 1.78. $C_2H_2O_2SFCl$. Calculated %: C 16.65; H 1.38.

Properties of fraction 2.

M.p. −22.0°, $n^{20}D$ 1.4341, $d^{20}_4$ 1.5247, $MR_D$ 24.58.
Found %: C 16.21, 16.24; H 1.77, 1.57. $C_2H_2O_2SFCl$. Calculated %: 16.65; H 1.38.

Besides this we also isolated a substance with b.p. 69.5-70° (25 mm).

$n^{20}D$ 1.4625, $d^{20}_4$ 1.5772, $MR_D$ 31.74. The chlorine split by the action of an equimolecular amount of triethylamine was 19.6, 20.1%.

Found %: F 7.66, 7.87. $C_2H_3O_2SFCl_2$. Calculated %: F 10.49.

This substance was evidently β,β-dichloroethanesulfonyl fluoride [1], which contained some amount of contaminants.

## SUMMARY

We have shown that the action of potassium fluoride on halogen substituted alkanesulfonyl chlorides can give sulfonyl fluorides of the unsaturated series and their halogen derivatives. By this method we have synthesized vinylsulfonyl fluoride and β-chlorovinylsulfonyl fluoride (in two stereoisomeric forms).

## LITERATURE CITED

[1] L. Z. Soborovskii, B. M. Gladshtein, M. I. Kiseleva and V. N. Chernetskii, Zh. O. Kh. 28, 1866 (1958).*

---

* Original Russian pagination. See C. B. Translation.

[2] I. L. Knuniants, O. V. Kil'disheva and E Bykhovskaia, Zh. O. Kh. 19, 101 (1949).*

[3] American patent 2653973 (1953); C. A. 48, 8813 (1954).

[4] R. Hübner, Lieb. Ann. 223, 198 (1884).

[5] A. Goldberg, J. Chem. Soc. 1945, 464.

[6] N. K. Kochetkov, Zh. O. Kh. 23, 744 (1953).*

[7] C. J Stehman, J. Am. Chem. Soc. 72, 4163 (1950).

[8] E. G. Focher, Dissertation, cited by J. B. Westerdyk, Inst. Petroleum, 36, 281 (1950).

[9] R. J. Muxer, J. Am. Chem. Soc. 75, 4094 (1953).

[10] B. C. Saunders, G. J. Stacey and J. G. Wilding, J. Chem. Soc. 1949, 775.

[11] E. F Landau, J. Am. Chem. Soc. 69, 1219 (1947).

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# THE HYDROLYSIS OF ESTERS OF AROMATIC SULFONIC ACIDS

## V. THE HYDROLYSIS OF ESTERS OF BENZENESULFONIC ACID AND SUBSTITUTED PHENOLS

R. V. Vizgert

A number of factors are significant in the mechanism of hydrolysis of esters: 1) conditions of hydrolysis (nature of catalysis, solvent, etc.)[1-3]; 2) acidic properties of the constituent acid and alcohol [4]; 3) spatial distribution of branching substituents in acyl or alkyl radicals of the ester [5-7].

Increase in the acidic properties not only of the acid, but also of the alcohol increases the rate of hydrolysis [8-10], and also in a number of cases changes the mechanism of hydrolysis. In esters of carbonic acid with aliphatic and aromatic alcohols and phenols, the bond is broken at the acyl [11-13, 35]. Esters of acids of medium strength, such as phosphoric [14], nitrous [4], and aliphatic alcohols are hydrolyzed at the acyl or alkyl bond depending on the medium. Esters of strong acids like $HClO_3$ [4], benzenesulfonic [15-17] and aliphatics are hydrolyzed only on the alkyl.

The results of previous work [18-20] on the study of the effect of electrophilic and nucleophilic substituents on the rate of hydrolysis of alkyl- and arylsulfonates which contain substituents in benzenesulfonic acid show different mechanisms for their hydrolysis [21]. The behavior of alkyl- and arylsulfonates in other reactions, such as reaction with water [22], alcohols [23], phenols [24, 25], amines [26, 27], and the action of hydrogen at the moment of its evolution [28], also show differences in the lability of the bonds in alkyl- and arylsulfonates. It is interesting to see what is the effect on reaction rate and mechanism of hydrolysis of arylsulfonates depending on the introduction of different substituents in the phenol. When substituents are introduced into benzenesulfonic acid the properties of the latter are changed slightly, while electrophilic and nucleophilic substituents in the phenol should change the dissociation constant of the phenol sharply, and hence should have considerable effect on the rate of hydrolysis of the arylsulfonate. For this study we chose esters of benzenesulfonic acid and phenol with substituents in the phenol and in the sulfonic acid: o-$CH_3$, p-Cl, p-$NO_2$, 2,4-$(NO_2)_2$. The results of the experiments agreed with the data from previous work.

## EXPERIMENTAL

Esters of benzenesulfonic acid with p-Cl, p-$NO_2$, and o-$CH_3$ substituted phenol were obtained by reaction of the substituted phenol with benzenesulfonic acid in an aqueous alkali medium with subsequent isolation and recrystallization [29]. The ester of 2,4-dinitrobenzenesulfonic acid and phenol was obtained from the corresponding sulfonyl chloride, which was kindly prepared for us by A. I. Tolmachev, and sodium phenolate in anhydrous alcohol [30]. The ester of 2,4-dinitrophenol and benzenesulfonic acid was obtained from the corresponding phenolate and benzenesulfonyl chloride in anhydrous alcohol. The melting points of the esters are given in Table 1.

Hydrolysis was carried out in a 70% water-dioxane medium with alkali at 50 and 70°. The initial concencentration of ester was 0.012 g mole/liter, and of KOH 0.033-0.035 g mole/liter. Hydrolysis of the ester from benzenesulfonic acid and 2,4-dinitrophenol and the ester from 2,4-dinitrobenzenesulfonic acid and phenol, because of the great rapidity, were carried out at 0 and 15°, and the initial concentration of ester was 0.0031 g mole/liter and of alkali 0.0084 g mole/liter (because of the small concentrations of ester and alkali, we used a double sample for titration).

TABLE 1

| Meaning of X and Y in the formula $YC_6H_4SO_2OC_6H_4X$ X | Y | Melting point |
|---|---|---|
| H | H | 35—36° [27] |
| 4-Cl | | 20—22 [29] |
| $4\text{-}NO_2$ | | 84—85 |
| $2\text{-}CH_3$ | | 39—40 |
| $2,4\text{-}(NO_2)_2$ | | 118—119 |
| H | $2,4\text{-}(NO_2)_2$ | 115—116 [34] |

The rate of hydrolysis was determined by titrating the excess acid with alkali in the presence of methyl red [18-20]. For a more detailed description of the method, see [8].

The rate constants of the hydrolysis were calculated by the equation of the second order with account taken of the double cost of alkali: $dx/dt = k(a-2x)(b-x)$, where: $a$ is concentration of alkali and $b$ is concentration of ester. The energy of activation was calculated by the Arrhenius equation:

$$E = \frac{(\log k_2 - \log k_1) \cdot 4.575 \cdot T_1 \cdot T_2}{T_2 - T_1}$$

The pre-exponential factor was calculated by the equation $k = Pzc^{-E/RT}$.

The dimensions of the values were: $k$ in liter/mole sec, E in cal/mole, $\log P_a$ in liter/mole sec.

TABLE 2

| 30° | | | | 50° | | | |
|---|---|---|---|---|---|---|---|
| $t$ (min) | $a-2x$ | $b-x$ | $k$ | $t$ (min) | $a-2x$ | $b-x$ | $k$ |
| 0 | 0.0353 | 0.0125 | — | 0 | 0.0353 | 0.0125 | — |
| 7 | 0.0309 | 0.0102 | 0.0161 | 3 | 0.0275 | 0.0085 | 0.0733 |
| 10 | 0.0290 | 0.0093 | 0.0152 | 9 | 0.0195 | 0.0045 | 0.0727 |
| 16 | 0.0263 | 0.0079 | 0.0153 | 13 | 0.0167 | 0.0030 | 0.0793 |
| 24 | 0.0237 | 0.0066 | 0.0152 | 19 | 0.0146 | 0.0021 | 0.0753 |
| 32 | 0.0210 | 0.0053 | 0.0165 | 26 | 0.0134 | 0.0015 | 0.0683 |
| 45 | 0.0191 | 0.0043 | 0.0154 | 40 | 0.0116 | 0.0006 | 0.0885 |
| | | $k_{av}$ | 0.0156 | | | $k_{av}$ | 0.0762 |

TABLE 3

| 50° | | | | 70° | | | |
|---|---|---|---|---|---|---|---|
| $t$ (min) | $a-2x$ | $b-x$ | $k$ | $t$ (min) | $a-2x$ | $b-x$ | $k$ |
| 0 | 0.0353 | 0.0125 | — | 0 | 0.0353 | 0.0125 | — |
| 400 | 0.0328 | 0.0111 | 0.000132 | 60 | 0.0326 | 0.0110 | 0.00088 |
| 770 | 0.0313 | 0.0104 | 0.000116 | 225 | 0.0284 | 0.0089 | 0.00074 |
| 1355 | 0.0282 | 0.0089 | 0.000132 | 345 | 0.0258 | 0.0076 | 0.00089 |
| 2135 | 0.0256 | 0.0076 | 0.000129 | 444 | 0.0239 | 0.0066 | 0.00082 |
| 2790 | 0.0237 | 0.0066 | 0.000131 | 520 | 0.0223 | 0.0059 | 0.00084 |
| | | $k_{av}$ | 0.000129 | | | $k_{av}$ | 0.00083 |

The results of several typical experiments on the hydrolysis of p-nitrophenyl benzenesulfonate and o-cresyl benzenesulfonate are given in Tables 2 and 3. In Table 4 we give the basic data on the hydrolysis of the arylsulfonates which we studied in this work.

For comparison of the effects of the same substituent in the benzene ring of the acid and of the alcohol on the rate of hydrolysis of the arylsulfonates, the results of the present study are compared to the kinetic data from previous work (Table 5).

TABLE 4

| Value of X and Y in formula $YC_6H_4SO_2OC_6H_4X$ |  | $k_5 \cdot 10^3$ | $k_{15} \cdot 10^3$ | $k_{50} \cdot 10^3$ | $k_{70} \cdot 10^3$ | $E$ | lg $P_z$ |
|---|---|---|---|---|---|---|---|
| X | Y |  |  |  |  |  |  |
| 2-$CH_3$ | H | — | — | 0.129 | 0.86 | 20880 | 10.24 |
| H |  | — | — | 0.374 | 1.900 | 17860 | 8.66 |
| 4-Cl |  | — | — | 2.47 | 11.23 | 16730 | 8.77 |
| 4-$NO_2$ |  | — | — | 76.65 | — | 15290 | 9.23 |
| 2,4-$(NO_2)_2$ |  | 339.0 | 830.0 | — | — | 9350 | 7.02 |
| H | 2,4-$(NO_2)_2$ | 38.0 | 183.0 | — | — | 16360 | 11.68 |

## Discussion of Results

Electrophilic and nucleophilic substituents act in the same direction on the rate of hydrolysis, independent of their location in the benzene ring of the phenol or the benzenesulfonic acid (in Table 5 the constants for the hydrolysis of arylsulfonates are compared with the dissociation constants of the substituted phenols).

If the order of effect of the different substituents is the same, yet the relative magnitude of the effect of each of the substituents is different and depends on where the substituent is found: in the benzene ring of the acid or of the alcoholic constituent. Electrophilic substituents in the phenolic benzene ring have a greater effect on the rate of hydrolysis of arylsulfonates than when the corresponding substitution is in the benzenesulfonic acid (p-Cl, p-$NO_2$). The effect of electron donor substituents transmitted through the benzene ring of the phenol is weaker than the effect of these substituents in the benzene sulfonic acid. If we consider that in hydrolysis of arylsulfonates the active reaction center is the sulfur of the sulfonyl group, then the greater effect of the electrophilic substituents in the benzene ring of the phenol can be explained by the presence on the oxygen of two pairs of p-electrons which are united to the electrons of the benzene ring. Change in the energy of activation and the probability factor correspond to the change found in the rate constant. The effect of substituents in the ortho, meta, and para positions differs depending on whether the substituent is in the benzene ring of the acid or alcoholic portion.

In esters of benzenesulfonic acid and substituted phenols the nitro group follows this order in its effect on rate of hydrolysis: o-$NO_2$ > p-$NO_2$ > m-$NO_2$, and for esters of phenol and substituted benzenesulfonic acids, a different order: p-$NO_2$ > m-$NO_2$ > o-$NO_2$. Thus, the nitro group in the ortho position in benzenesulfonic acid decreases the rate of hydrolysis of arylsulfonates and aromatic sulfonyl chlorides [20], while the nitro group in the ortho position in phenols has a favorable effect, showing only its electronic action and not steric hindrance.

The methyl group in its lessening effect on the rate of hydrolysis of esters of benzenesulfonic acid and substituted phenols stands in the order o-$CH_3$ > p-$CH_3$ > m-$CH_3$.

The decrease in rate of hydrolysis shown by the methyl group in the ortho position can come from its electronic influence and not from a spatial effect.

The accumulation of electronegative nitro groups in benzene sulfonic acid, and especially in phenol, sharply increases the rate of alkaline hydrolysis. The ester of 2,4-dinitrophenol with benzenesulfonic acid, as distinct from the corresponding unsubstituted ester of phenol, and even from the ester of 2,4-dinitrobenzenesulfonic acid with phenol, is hydrolyzed by water, which does not occur with the latter two. When a water-dioxane solution of the ester of 2,4-dinitrophenol and benzenesulfonic acid is heated for 45 hours on the water bath at 80°, it is 45% hydrolyzed, and when heated in a sealed tube at 120° for 37 hours, 60%. Under these conditions the ester from 2,4-dinitrobenzenesulfonic acid and phenol gave only a trace (3-5%) of phenol. When phenyl benzenesulfonate was heated for 140 hours at 120° it did not even give a trace of phenol. The presence of acid as a catalyst in all cases did not affect the rate of hydrolysis. In this respect esters of 2,4-dinitrophenol and benzenesulfonic acid resemble the alkyl esters of benzenesulfonic acid (which are hydrolyzed by water and the rate of hydrolysis is considerably increased by the presence of alkali and not by the presence of acid). It is possible that further evidence of this resemblance will be found in the mechanism of hydrolysis. Comparison

TABLE 5

| Value of X | $C_6H_5SO_2OC_6H_4X$ |  |  | $XC_6H_4SO_2OC_6H_5$ |  |  | $XC_6H_4SO_2OC_6H_4SO_2C_6H_4OH$ |  |  | $XC_6H_4OH$ |
|---|---|---|---|---|---|---|---|---|---|---|
|  | $k_{50} \cdot 10^3$ | $E$ | lg $P_Z$ | $k_{50} \cdot 10^3$ | $E$ | lg $P_Z$ | $k_{50} \cdot 10^3$ | lg $P_Z$ | $E$ | dissociation constant |
| 2-$CH_3$ | 0.129 | 20880 | 10.24 | — | — | — | — | — | — | $6.3 \cdot 10^{-11}$* |
| 4-$CH_3$ | 0.184 | 18500 | 8.78 | 0.145 | 18650 | 8.78 | — | — | — | $6.7 \cdot 10^{-11}$ |
| 3-$CH_3$ | 0.263 | 18320 | 8.82 | — | — | — | — | — | — | $9.8 \cdot 10^{-11}$ |
| H | 0.374 | 17860 | 8.66 | 0.374 | 17860 | 8.66 | 15.45 | 8.64 | 15460 | $1.0 \cdot 10^{-10}$ |
| 4-Cl | 2.47 | 16730 | 8.77 | 1.120 | 17190 | 8.72 | 21.70 | 8.81 | 15470 | — |
| 2-$NO_2$ | 134.9 | 15980 | 9.95 | 7.34 | 16340 | 8.92 | — | — | — | $7.5 \cdot 10^{-8}$** |
| 4-$NO_2$ | 76.65 | 15290 | 9.23 | 26.3 | 13160 | 7.40 | — | — | — | $9.6 \cdot 10^{-8}$ |
| 3-$NO_2$ | 31.5 | 15450 | 8.95 | 11.44 | 15200 | 8.35 | 171.2 | 9.33 | 14890 | $5.3 \cdot 10^{-9}$ |
| 2,4-$(NO_2)_2$ | $k_0 = 339$ | 9350 | 7.02 | $k_0 = 38.0$ | 16350 | 11.68 | — | — | — | $1.0 \cdot 10^{-4}$ |
| $HOC_6H_4SO_2$ | 15.45 | 15460 | 8.64 | — | — | — | — | — | — | $2.7 \cdot 10^{-8}$*** |
| $C_6H_5SO_2$ | 23.25 | 15110 | 8.60 | — | — | — | — | — | — | $1.4 \cdot 10^{-8}$ |

*[31]. **[32]. ***[33].

of the rate constant of the hydrolysis with the dissociation constant of the corresponding phenol shows that increase in acid properties of the alcohol increases the rate of hydrolysis (Table 5). An analogous relation between rate of hydrolysis and dissociation constant occurs in the esters of benzoic acid with substituted phenols [10].

The parallel between the dissociation and hydrolysis constants confirms the assumption of Hammett [13] of the constancy of the effect of substituents transmitted through a benzene ring in different types of chemical reactions in which the substituted benzene ring takes part. However, we could not calculate the reaction constants of the hydrolysis of esters of benzenesulfonic acid with substituted phenols because of the presence of the ester oxygen which strengthened or weakened the action of the substituents.

The experimental data which we obtained (greater effect of substituents in the alcoholic portion on rate of hydrolysis of aryl sulfonates compared to the corresponding substituents in the acid portion; presence of an ortho effect when the substituent is introduced into esters of substituted benzenesulfonic acids and its absence when introduced into esters of benzenesulfonic acid with substituted phenols) confirms the mechanism of hydrolysis of aryl sulfonates with rupture of the bond sulfur-oxygen, so that the ester oxygen remains on the side of the phenolic residue, and the active center of the reaction is the sulfur of the sulfonyl group.

## SUMMARY

1. We have studied the rate of alkaline hydrolysis of six esters of benzenesulfonic acid and substituted phenols.

2. Increased acidic properties of the substituted phenols increases the rate of hydrolysis of the corresponding esters of benzenesulfonic acid.

3. Electronegative substituents show a great effect on the rate of hydrolysis when in the alcoholic but not when in the acid portion of the ester.

4. Substituents in the ortho position in the benzene ring of the phenol do not show a steric effect.

5. The results confirm the mechanism of hydrolysis of aryl sulfonates in which the active center of the reaction is the sulfur of the sulfonyl group.

6. The ester of 2,4-dinitrophenol and benzenesulfonic acid as distinct from the other known esters of substituted phenols, is hydrolyzed by water.

## LITERATURE CITED

[1] N. Brown, Hudson, J. Chem. Soc. 1953, 883.

[2] E. Tommila, Acta chem. Scand. 9, 975 (1955).

[3] E. Tommila and E. Merrikallio, Suom. kemist, No. 12, 225 (1953).

[4] M. Anber, I. Dostrowsky, D. Samuel and A. Laffe, J. Chem Soc. 1954, 3603.

[5] V. Stimson, J. Chem. Soc. 1955, 2010, 2673.

[6] H. Goering, T. Rubin and M. Newman, J. Am. Chem. Soc. 76, 787 (1954).

[7] R. Dabby and A. Davies, J. Chem. Soc. 1953, 3619.

[8] Ia. Berkman and R. Vizgert. Ukrain, Khim. Zhur. 20, 264 (1954).

[9] E. Tommila and C. Hinchelwood, C. A. 33, 1199 (1939).

[10] L. Perenyi, Acta physiol. Acad. Sci. Hung. 5, No. 1-2, 103 (1954).

[11] C. Ingold, J. Chem. Soc. 1932, 756.

[12] I. Day and C. Ingold, Trans. Faraday Soc. 37, 686 (1941).

[13] L. P. Hammett, Physical Organic Chemistry, N. J. 350 (1940).

[14] K. Oldham, B. Silver and C. Vernon, Chem. a. Ind. No. 27, 760 (1955).

[15] L. Demeny, Rec. trav. chim. 50, 60 (1931).

[16] R. Robertson, Can. J. Chem. 31, 589 (1953).

[17] E. Tommila and M. Lindholm, Acta Chem. Scand. 4, 491 (1951).

[18] R. Vizgert, Ukrain. Khim. Zh. 20, 272 (1954).

[19] R. Vizgert and E. Savchuk, Zh. O. Kh. 26, 2261, 2268 (1956).*

[20] R. Vizgert and E. Savchuk, Nauch. Zap., L'vovsk, Politekh. Inst. 22, ser. khim.-tekh. No. 2, 39, 1956.

[21] C. A. Bunton and Frei, J. Chem. Soc. 1951, 1972.

[22] E. Tommila and O. Heinonen, Suomen kem. 27, No. 4, 27 (1954).

[23] M. Morgan and L. Gretcher, J. Am. Chem. Soc. 70, 375 (1948).

[24] F. Drahowzal and D. Klamann, Monatsh. 82, 588 (1951).

[25] A. Kostsova, E. Fedosova and I. Rozhkova, Tr. Voronezhsk. Gos. Univ. 28, 28 (1953).

[26] R. Autenrieth and Bernheim, Ber. 37, 3803 (1904).

[27] K. Otto, Ber. 19, 1832 (1886).

[28] F. Kenner and Murray, J. Chem. Soc. 1950, 406.

[29] G. Georgescu, Bull. Soc. Stiinte, Bucuresci, 8, 669 (1900).

[30] Ch. Suter, Chemistry of Organic Sulfur Compounds, part 2, 372 (1951).**

[31] Beilst, VI, 349, 373, 389 (1923).

[32] L. Pauling, Nature of the Chemical Bond, 205 (1947).***

[33] Ia. Berkman and L. Polonskaia, Nauch. Zap. L'vovsk, Politekh. Inst. 22, ser. khim.-tekh. No. 2, 49, (1956).

[34] A. I. Kiprianov and A. I. Tolmachev, Zh. O. Kh. 27, 486 (1957).*

[35] S. N. Baranov and R. V. Vizgert, Zh. O. Kh. 27, 209 (1957).*

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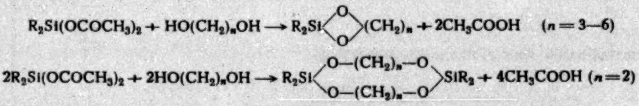
***Russian translation.

# STUDIES IN THE FIELD OF ALKOXYSILANES

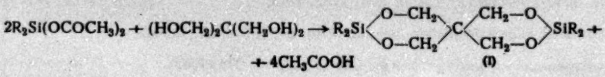
## XI. REACTION OF DIALKYLDIACETOXYSILANES WITH GLYCEROL AND PENTAERYTHRITOL*

V. P. Davydova and M. G. Voronkov

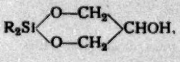
Earlier [2] we showed that dialkyldiacetoxysilanes react with glycols to form cyclic ethers of the dialkylsilanediols or their dimers.



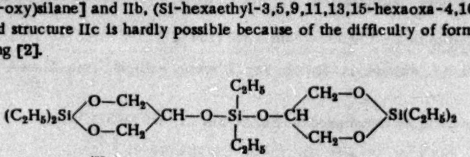
It appeared interesting to us to extend their reaction to polyatomic alcohols, especially to glycerol and pentaerythritol. We showed that dialkyldiacetoxysilanes react smoothly with pentaerythritol with the formation of the previously unknown spirocyclic ethers of dialkylsilanediol according to the scheme:



Thus, for example when pentaerythritol reacts with dimethyldiacetoxysilane, we get 88% of crystalline 3,3,9,9-tetramethyl-2,4,8,10-tetraoxa-3,9-disilaspiro(5,5)undecane (I).

The reaction of dialkyldiacetoxysilanes with glycerol is more complex and does not lead to the formation of 2-sila-1,3-dioxolane derivatives of the type  which are described in the patent literature [3].

When diethyldiacetoxysilane reacts with glycerol we find an 80% yield of a compound which corresponds to the formula $C_{18}H_{40}O_6Si_3$ (II), for which two structures are equally possible: IIa, [diethyl-bis-(2,2-diethyl-1,3-dioxa-2-silacyclohex-5-oxy)silane] and IIb, (Si-hexaethyl-3,5,9,11,13,15-hexaoxa-4,10,14-trisilabiscyclo[5,5,3]-pentadecane). The third structure IIc is hardly possible because of the difficulty of formation of a five membered 2-sila-1,3-dioxolane ring [2].



(IIa)

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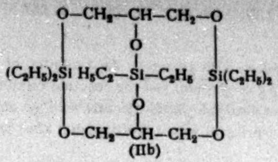
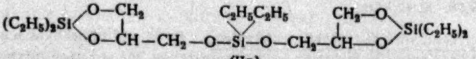
* Previous communication, see [1].



(IIb)



(IIc)

In contrast to this, when dimethyldiacetoxysilane reacted with glycerol, in all the experiments we obtained an easily polymerized substance of the formula $C_7H_{16}O_5Si$ which contained two hydroxyl groups and one acetoxy group united with a carbon atom.* One of the hydroxyl groups occurs on a silicon atom, as the infrared spectrum of the substance shows.** The spectrum has a very strong band at 3485 $cm^{-1}$ which belongs to an associated OH group. In the spectrum of a 0.5% solution of the substance in $CCl_4$ the nature of the band is little changed (there is a slight increase in frequency) which evidently shows the presence of an intramolecular hydrogen bond. There is complex absorption in the 880-790 $cm^{-1}$ region. However, in a 10% solution of the substance in pyridine, one of the bands ($\sim 815$ $cm^{-1}$) is shifted because at this place passage increases. Usually the bands belonging to the oscillation of the valence group Si–OH behave thus.

All these results show that the product of the reaction of dimethyldiacetoxysilane with glycerol is dimethyl-(2-hydroxy-3-acetoxypropoxy)silanol (III). The formation of (III) can be presented in the following scheme

$$\begin{gathered}(CH_3)_2Si(OCOCH_3)_2 + HOCH_2CHOHCH_2OH \rightarrow \\ \rightarrow (CH_3)_2Si(OCOCH_3)OCH_2CHOHCH_2OH + CH_3COOH \rightarrow \\ \rightarrow (CH_3)_2Si(OCOCH_3)OCH_2CHOHCH_2OCOCH_3 + H_2O \rightarrow \\ \rightarrow \underset{(III)}{(CH_3)_2Si(OH)OCH_2CHOHCH_2OCOCH_3} + CH_3COOH,\end{gathered}$$

or as a direct intramolecular rearrangement of the primary reaction product (cf [4]).

$$(CH_3)_2Si(OCOCH_3)OCH_2CHOHCH_2OH \rightarrow \underset{(III)}{(CH_3)_2Si(OH)OCH_2CHOHCH_2OCOCH_3}$$

The occurrence of an acetoxy group in compound (III) on the primary carbon atom is indicated since glycerol usually acetylates in the $\alpha$-position.

## EXPERIMENTAL

The starting dialkyldiacetoxysilanes were described earlier [5]. Glycerol was purified by vacuum distillation and had b.p. 155° (5 mm), $n^{20}D$ 1.4743. Pentaerythritol was recrystallized from water then dried in a vacuum oven over $P_2O_5$ (m.p. 260.5°).

Reaction of dimethyldiacetoxysilane with pentaerythritol. 52.9 g of dimethyldiacetoxysilane was added to 20.4 g of pentaerythritol and the mixture was stirred at 80-90° for 1 hour. The acetic acid which formed was distilled off in a vacuum and the residue was distilled at ordinary pressure. Yield of (I) with b.p. 243-245° (749 mm) was 32.8 g (88%). After two distillations in a vacuum, m.p. 136°.

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*A substance which contains an acetoxy group on a silicon atom is easily hydrolyzed by water or aqueous alkali with splitting of the acetoxy group, which does not occur in this case.

**The authors are grateful to Ia. I. Ryskin for the infrared spectrum and its interpretation.

Found %: C 43.21, 43.24; H 7.97, 8.09; Si 22.21, 22.31. M 252.0, 254.2. $C_9H_{20}O_4Si_2$. Calculated %: C 43.51; H 8.11; Si 22.61. M 248.44.

Reaction of diethyldiacetoxysilane with glycerol. To a solution of 39.8 g of diethyldiacetoxysilane in 100 ml of absolute ether was added 12.0 g of glycerol and the reaction mixture was stirred for 3 hours. After distillation of the ether, the residue was vacuum distilled. Besides acetic acid we obtained 22.8 g of (II) with b.p. 230-245° (14 mm). Yield 80%. A colorless, viscous liquid with a boiling point after repeated distillation of 230-233° (14 mm).

$d^{20}_4$ 1.0521, $n^{20}_D$ 1.4605.
Found %: C 49.86, 49.99; H 9.50, 9.69; Si 19.27, 19.19. M 439.9, 433.1. $C_{18}H_{40}O_6Si_3$. Calculated %: C 49.50; H 9.23; Si 19.29. M 436.78.

Reaction of glycerol with dimethyldiacetoxysilane. To 67 g of dimethyldiacetoxysilane was added with stirring 23 g of glycerol. After stirring 10 minutes at room temperature, the reaction mixture warmed spontaneously to 50°. With further stirring it set to a clear, viscous mass which was dissolved by adding 70 ml of absolute ether. After distillation of the ether the reaction mass was distilled in a vacuum. We thus obtained 41 g of (III) (yield 79% calculated on the starting glycerol). B.p. 102-133° (10 mm); after a second distillation, b.p. 125-130° (10 mm).

$d^{20}_4$ 1.1432, $n^{20}_D$ 1.4450.
Found %: C 41.30, 41.60; H 7.87, 8.03; Si 13.48, 13.29; $OCOCH_3$ 27.95, 28.07; H(O) 0.74. M 313.2, 325.2. $C_7H_{16}O_5Si$. Calculated %: C 40.36; H 7.74; Si 13.48; $OCOCH_3$ 28.36; H(O) 0.97. $(C_7H_{16}O_5Si)_{1.5}$. Calculated: M 312.44.

The substance was a colorless, viscous liquid, especially unstable when kept and easily polymerized, which makes its analysis difficult. The substance was dissolved in water; the water solution had a neutral reaction. After 12 hours in a sealed ampoule, the substance was converted into a clear, glassy resin. This resin distilled without decomposition at 162-184° (4 mm), passing over as a viscous liquid which quickly set again to the resin with the same properties. The results of a molecular weight determination in dioxane showed that the substance was associated (degree of association 1.5).

In another experiment, in which the molar ratio of the starting substances was 1 : 1, we also obtained substance (III) with a yield of 72%. B.p. 155-160° (15 mm), $n^{20}_D$ 1.4460.

## SUMMARY

The reaction of dialkyldiacetoxysilanes with pentaerythritol leads to formation of a spirocyclic ether of dialkylsilanediol. Diethyldiacetoxysilane and dimethyldiacetoxysilane react differently with glycerol, forming in the first case a bicyclic ether of diethylsilanediol, and in the second, an acyclic monoether of dimethylsilanediol with α-acetyl.

## LITERATURE CITED

[1] M. G. Voronkov and B. N. Dolgov, Izv. AN SSSR, OKhN, 1957, 1128.*

[2] M. G. Voronkov, V. P. Davydova and B. N. Dolgov, Izv. AN SSSR, OKhN 1958, 698. *

[3] English patent 749958 (1956), C. A. 50, 19123 (1956).

[4] B. N. Dolgov, V. P. Davydova and M. G. Voronkov, Zh. O. Kh. 27, 921 (1957).*

[5] B. N. Dolgov, V. P. Davydova and M. G. Voronkov, Zh. O. Kh. 27, 1593 (1957).*

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# THE SPLITTING OF MACROTOMINIC ACID AND ACIDS FROM HELIOSUPINE IN CAUSTIC ALKALI SOLUTIONS

S. I. Denisova, M. F. Petrova and G. P. Men'shikov

Macrotominic acid was first observed in a study of the alkaloid macrotomine as an ester of this acid and the aminoalcohol trachelanthamidine. However, the acid was so strongly decomposed when the alkaloid was saponified by caustic alkalis that it could not be obtained in pure form. Therefore, for a study of its structure the free acid was not used, but macrotomine itself; and on the basis of a study of the products of its oxidative decomposition by its reaction with iodic acid, it was shown with great probability that macrotominic acid has the structure 2-methyl-2,3,4-trihydroxypentane-3-carboxylic acid (I) [1]. Thus, the structure of macrotominic acid differs from lasiocarpic and only in that it has a hydroxyl group in position 4 instead of a methoxyl [2].

Lasiocarpic acid also is not obtained by saponifying the alkaloid, but it can easily be obtained in pure form by reducing lasiocarpine with a platinum catalyst. This reduces the allyl hydroxyl group which is esterified with lasiocarpic acid.

Macrotomine, an ester of the saturated amino alcohol trachelanthamidine, cannot be catalytically reduced to give a free acid of the structure 2-methyl-2,3,4-trihydroxypentane-3-carboxylic acid. However, such a possibility exists, due to the discovery of the new alkaloid, heliosupine. This alkaloid is very close in structure to lasiocarpine and differs from it only in that the primary hydroxyl group of heliotridine (allyl) is esterified not with lasiocarpic acid, but with an acid which has the same structure as macrotominic acid [3]. Naturally, we can expect to obtain from this alkaloid the free acid under conditions for obtaining lasiocarpic acid from lasiocarpine.

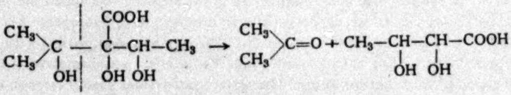
Actually, when heliosupine is reduced with a platinum catalyst it gives a free acid which is characterized as the quinine salt, m.p. 186° (the free acid does not crystallize).

From the products of splitting macrotominic acid obtained by alkaline hydrolysis of the alkaloid macrotomine was isolated acetone and an optically inactive acid with the composition $C_4H_8O_4$. This was isolated as its quinine salt with m.p. 173-174° and with $[\alpha]_D$ −104° (water).

These constants are very close to those for the quinine salt of the high melting inactive form of $\alpha,\beta$-dihydroxybutyric acid (m.p. 174°, $[\alpha]_D$ −108° [4]). However, the latter in the free form is described as a well crystallized substance with a melting point about 80°, while our acid does not crystallize.

To confirm the composition of our acid we must find a simpler salt with a lower molecular weight than the quinine salt. The well crystallized sodium salt was such a one; analysis of this salt confirms the composition $C_4H_8O_4$ for the acid, that is, the composition of dihydroxybutyric acid.

A comparison of these results with the structural formula for macrotominic acid gives the important conclusion that splitting of the latter takes place by rupture of the C−C bond between the 2nd and 3rd carbon atoms, occurring because of transfer of a hydrogen atom from the hydroxyl group in position 2 to the carbon atom in position 3.



$$(CH_3)_2C(OH)-C(COOH)(OH)-CH(OH)-CH_3 \rightarrow (CH_3)_2C{=}O + CH_3-CH(OH)-CH(OH)-COOH$$

(I)

As our investigation showed, lasiocarpic acid undergoes an analogous split. Also we found for lasiocarpic acid that the rate of its splitting depends to a considerable extent on whether the free acid (more exactly, its salt) or its ester is submitted to the action of an alkaline solution. In the case of the ester splitting goes about 200 times faster than in the case of the salt [5].

Obtaining a free acid with the structure of 2-methyl-2,3,4-trihydroxypentane-3-carboxylic acid from heliosupine made it possible to confirm this finding and to judge the degree of its splitting by the amount of acetone evolved. It was shown that this acid is also split very slowly when it is heated in an alkaline solution, while the analogous action of alkali on macrotomine and heliosupine gives a much faster splitting.

The very small amount of heliosupine which we had at our disposal did not permit us to obtain sufficient free acid to synthesize its pure methyl ester. The inability to crystallize it also made its purification difficult. Yet even the work with the impure ester obtained by the action of diazomethane on the acid showed that the rate of its splitting was increased compared to that of the free acid and was very close to the rate of splitting of the methyl ester of lasiocarpic acid.

## EXPERIMENTAL

Splitting of macrotominic acid in the saponification of macrotomine. 5 g of the alkaloid was dissolved in 40 ml of 1 N sodium hydroxide solution and the solution was heated for 1 hour in a sealed ampoule on a boiling water bath. Then the ampoule was carefully cooled and its contents transferred to a Wurtz flask. The ampoule was washed with 20 ml of water, the wash water was combined with the alkaline solution, and 25 ml of water was distilled from the combined solutions in order to estimate the acetone which was formed. Concentrated hydrochloric acid was added to the distillate in such amount that the acid concentration was about that of a 2N solution. Then a solution saturated at 20° with 2,4-dinitrophenylhydrazine was added to the 2 N hydrochloric acid solution to complete precipitation of the acetone. We obtained 3.55 g (89.9%) of acetone dinitrophenylhydrazone. The residual alkaline mother liquors after the acetone had been distilled off were extracted with chloroform to complete removal of the amino alcohol (trachelanthamidine), and after carbon dioxide gas has been passed in, the water was completely distilled off in a vacuum. The dry residue was extracted with boiling anhydrous alcohol. The inorganic salts were filtered from the alcohol solution, and the solvent was distilled from it. The residue was dissolved in 50 ml of water and the solution was passed through a column of ion exchange resin (cationite p, phenolic). After the solution was dried in a vacuum, the quinine salt was obtained from the noncrystallizing acid. For this the acid was dissolved in a small amount of alcohol and to the solution dry quinine was added until the acid reaction disappeared. The salt was separated from the solution by adding a large amount of dry ether. The precipitate was washed with ether and recrystallized from dry acetone. After two recrystallizations the salt melted at 173-174°, $[\alpha]_D^{16}$ −104° (c 5.00, water).

Found %: C 64.74, 64.76; H 7.48, 7.52; N 6.28. $C_{24}H_{32}O_6N_2$. Calculated %: C 64.82; H 7.27; N 6.30.

Sodium salt. 1.2 g of the quinine salt was dissolved in 30 ml of water and the solution was passed through a column filled with ion exchange resin (cationite p, phenolic). The resulting acid solution was treated with an excess of sodium bicarbonate and evaporated to dryness in a vacuum. The dry residue was extracted with boiling anhydrous alcohol. The alcohol solution was filtered and concentrated to small volume. Addition of ether to the concentrated alcohol solution gave a crystalline precipitate (after recrystallization from alcohol, white, glittering plates).

Found %: C 33.35, 33.63; H 4.85, 4.73. $C_4H_7O_4Na$. Calculated %: C 33.80; H 4.92.

The salt was optically inactive.

Judging by the amount of acetone formed in the saponification of heliosupine we concluded that in this case the acid underwent an analogous splitting.

Obtaining a free acid from heliosupine. Heliosupine, obtained from 10 g of the crystalline picrate, was dissolved in 40 ml of 0.5 N hydrochloric acid solution and to the solution was added the catalyst (from 1 g of $H_2PtCl_6$) and the mixture was shaken at a small excess pressure in an atmosphere of hydrogen. About 3 g moles of hydrogen were rapidly absorbed. The acid solution was filtered from the catalyst, neutralized with soda, and evaporated dry. The residue was extracted with boiling anhydrous alcohol. The alcohol was completely distilled from the solution and the residue was dissolved in 150 ml of water. The water solution was passed through a column with a cationite resin (espatite). After the passage of all the solution, the column was washed with water. The solution and the wash water were combined and evaporated dry in a vacuum. There remained a colorless, noncrystalline mass whose water solution rotated a plane of polarized light to the right.

To characterize the noncrystalline free acid we prepared its quinine salt. To an alcohol solution of the acid we gradually added dry quinine to a full alkaline reaction and precipitated the quinine salt with absolute ether. After reprecipitation from alcohol solution by ether the salt appeared as snow white, silky needles with m.p. 186°, $[\alpha]_D^{20}$ −105° (c 6.46, alcohol).

Found %: C 64.34, 64.48; H 7.61, 7.66; N 5.74, 5.89; OH 17.23, 16.70. $C_{27}H_{38}O_7N_2$. Calculated %: C 64.47; H 7.62; N 5.57; OH 16.92.

*Splitting of the acid from heliosupine by alkaline solution.* 1 g of the acid obtained from the quinine salt by passing its water solution through a cationite resin (espatite) was heated in a sealed ampoule at 100° in 20 ml of 1 N sodium hydroxide for 4 hours. All further operations in the determination of the amount of acetone formed were carried out in the same way as in the case of splitting of macrotomine. We obtained 0.028 g (2.09%) of acetone 2,4-dinitrophenylhydrazone.

## SUMMARY

In the alkaline splitting of macrotomine and heliosupine which are esters of an acid with the structure 2-methyl-2,3,4-trihydroxypentane-3-carboxylic acid [1], the latter was quickly split into acetone and dihydroxybutyric acid. This splitting also occurs in the heating in alkaline solution of the free acid from heliosupine (more correctly, its salt) but it goes much more slowly (about 200 times less).

## LITERATURE CITED

[1] G. P. Men'shikov and M. F. Petrova, Zh. O. Kh. 22, 1457 (1952).*

[2] A. D. Kuzovskov, Dissertation, The Structures of the Alkaloids Heliotrine and Lasiocarpine, VNIKhFI (1948);** L. Drumond, Nature 167, 41 (1951).

[3] S. I. Denisova, G. P. Men'shikov and L. M. Utkin, DAN SSSR 98, 59 (1953).

[4] R. Fittig, Lieb. Ann. 268, 8 (1892); R. S. Morrell and E. K. Hanson, J. Chem. Soc. 85, 197 (1904); J. W. Glattfeld and W. G. Straitiff, J. Am. Chem. Soc. 60, 1384 (1937).

[5] M. F. Petrova, S. I. Denisova and G. P. Men'shikov DAN SSSR 114, 1073 (1957).*

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# INTERMEDIATE PRODUCTS IN THE CONDENSATION REACTION OF ISOAMYL ALCOHOL

V. I. Liubomilov and A. I. Kutsenko

In the reaction of isovaleric aldehyde with solutions of sodium isoamylate in isoamyl alcohol [1] two unsaturated alcohols are formed: 2,6-dimethyl-3-methylol-4-heptene and 2,6-dimethyl-3-methylol-3-heptene. From these alcohols there is gradually formed 2,6-dimethyl-3-methylolheptane, which is the condensation product of isoamyl alcohol in the presence of its alcoholate [2]. It is natural to expect that when the latter reaction proceeds, the intermediate products will be the same two unsaturated alcohols and not one, as had been assumed, for example, in the scheme suggested by one of us [3], and also in a very similar later scheme [4].

In the present work we carry out the condensation of isoamyl alcohol in the presence of its alcoholate and a dehydrogenation catalyst. Investigation of the reaction products showed that in them, besides the basic reaction product, 2,6-dimethyl-3-methylolheptane, there were present in about equal amounts both of the above mentioned unsaturated alcohols.

## EXPERIMENTAL

The condensation of isoamyl alcohol was carried out in the apparatus used by us for the condensation of n-butanol. It was filled with 2500 g of isoamyl alcohol, 90 g of sodium hydroxide, and 170 g of catalyst (nickel on aluminum oxide). The length of the condensation was 40 hours; the temperature of the reaction mass at the beginning of the process was 120°, and at the end, 137°. As a result of formation of the alcoholate and condensation of the alcohol, 168 g of water was formed; 93 liters of hydrogen were obtained. The reaction product was steam distilled and the distilled alcohols were separated from the water and from unreacted isoamyl alcohol (1359 g). Besides this, 24 g of isoamyl alcohol with a content of 44% isovaleric aldehyde was separated from the water layer after running the condensation.

Rectification of the condensation product. The alcohols obtained after distilling off the isoamyl alcohol, in the amount of 674 g, were carefully fractionated in a vacuum in a column filled with Raschig glass rings. The effectiveness of the column was about 20 theoretical plates. The resulting fractions were then rectified in a vacuum on a column with the effectiveness of 11 theoretical plates. In the fractions obtained by the second fractionation we determined the specific gravity, refractive index, and bromine and hydroxyl numbers, and from these data constructed a curve of distillation. On the basis of this curve we could determine the amounts of each of the alcohols which were formed. The yields of alcohols are given in the Table. The groups of fractions with

Alcohols Obtained by the Condensation of Isoamyl Alcohol

| Name of alcohol | Yield (in %) | Boiling point (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ |
|---|---|---|---|---|
| 2,6-Dimethyl-3-methylol-4-heptene | 105 | 201—202° (762) | 0.8348 | 1.4443 |
| 2,6-Dimethyl-3-methylol-3-heptene | 100 | 203.5—205 (748) | 0.8485 | 1.4520 |
| 2,6-Dimethyl-3-methylolheptane | 360 | 207.5—208 (729) | 0.8345 | 1.4369 |

similar properties were submitted to a supplementary vacuum rectification on a column in order to separate pure components. The properties of the resulting substances are given in the same table. The boiling points at atmospheric pressure were determined by distillation of the substances in a Wurtz flask.

2,6-Dimethyl-3-methylol-4-heptene. We obtained 35 g in pure form.

Found %: C 76.89; H 13.04; OH 10.51. Bromine No. 1032. $C_{10}H_{19}OH$. Calculated %: C 76.86; H 12.91; OH 10.89. Bromine No. 1024.

α-Naphthylurethane, m.p. 64.5-65°. Mixed m.p. with the form obtained earlier [1] gave no depression.

2,6-Dimethyl-3-methylol-3-heptene. We obtained 20 g in pure form.

Found %: C 76.64; H 12.83; OH 10.67. Bromine No. 1033. $C_{10}H_{19}OH$. Calculated %: C 76.86; H 12.91; OH 10.89. Bromine No. 1024.

2,6-Dimethyl-3-methylolheptane. We obtained it in small amount in comparatively pure form.

Found %: C 75.94; H 14.03; OH 10.51. Bromine No. 12. $C_{10}H_{21}OH$. Calculated %: C 75.88; H 14.01; OH 10.74. Bromine No. 0.

The major portion of the 2,6-dimethyl-3-methylolheptane, which contained small amounts of the unsaturated alcohols and higher boiling alcohols, was submitted to catalytic hydrogenation and subsequent rectification. We then obtained 2,6-dimethyl-3-methylolheptane with the following constants: $d^{20}_4$ 0.8345, $n^{20}D$ 1.4370.

The constants of all three alcohols were close to those found earlier [1].

## SUMMARY

We have studied the condensation of isoamyl alcohol in the presence of its alcoholate and a dehydrogenation catalyst. In the reaction product we find 2,6-dimethyl-3-methylolheptane and two isomeric unsaturated alcohols: 2,6-dimethyl-3-methylol-4-heptene and 2,6-dimethyl-3-methylol-3-heptene.

## LITERATURE CITED

[1] V. I. Liubomilov, Zh. O. Kh. 26, 2738 (1956).*

[2] M. Guerbet, Comptes rend. 128, 511 (1898).

[3] V. I. Liubomilov, Dissertation, Obtaining Pure 2-Ethylhexanol by Condensation of n-Butanol in the Presence of Its Alcoholate and a Catalyst, Moscow, 1950.**

[4] J. Boll and Bourgeois, Chim. et Ind. 68, 522 (1952).

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# TRICHLOROISOPHOSPHAZOACYLS OF THE AROMATIC SERIES

## A. V. Kirsanov and G. I. Derkach

There were prepared recently some trichloroisophosphazoacyls by the following reaction scheme:

$$RCONH_2 + PCl_5 \rightarrow 2HCl + RCON=PCl_3 \quad (1)$$

$$RCON=PCl_3 + HCOOH \longrightarrow HCl + CO + RCONHPOCl_2 \quad (2)$$

$$RCONHPOCl_2 + PCl_5 \longrightarrow POCl_3 + RCCl=NPOCl_2, \quad (3)$$

where: $R = CCl_3$ [1], $(C_6H_5)_2ClC$ & $p\text{-}NO_2C_6H_4$ [2].

It was interesting to determine whether or not reaction (3) is general or whether it is applicable only to carboxylic acids with a radical having clearly expressed electronegative character. It turned out that reaction (3) does have a general character for acids of the aromatic series. There was prepared with almost quantitative yields a number of trichlorophosphazoacyls of the type $RCCl=NPOCl_2$, where R = $C_6H_5$, $p\text{-}CH_3C_6H_4$, α- and β-$C_{10}H_7$, o- and $p\text{-}ClC_6H_4$, $2,4\text{-}Cl_2C_6H_3$, o-, m- and $p\text{-}O_2NC_6H_4$, $3,5\text{-}(O_2N)_2C_6H_3$ and $m\text{-}C_6H_4(CCl=NPOCl_2)_2$ (Table 1).

Reaction (3) proceeds considerably less rapidly and at a higher temperature than does reaction (1) [3]. The absorption of heat [4] which is characteristic of reaction (1) is not observed in reaction (3). The reaction (3) resembles in its character the reaction of phosphorus pentachloride with N,N-dialkylamides of carboxylic acids [5].

Trichloroisophosphazoacyls of the aromatic series are liquid or low melting crystalline substances. They lose phosphorus oxychloride on being heated and yield nitriles according to the scheme:

$$RCCl=NPOCl_2 \longrightarrow POCl_3 + RCN \quad (4)$$

However, reaction (4) proceeds considerably slower and at much higher temperatures than the thermal decomposition of trichlorophosphazoacyls [3] according to scheme (5) (Table 1 and Table 2).

$$RCON=PCl_3 \longrightarrow POCl_3 + RCN \quad (5)$$

Thus the jump of chlorine proceeds noticeably more difficultly than the jump of oxygen. This is evidently explained by the fact that in the reaction (5) there occurs a replacement of N=P bond by a thermodynamically much more advantageous O=P bond, while in reaction (4) there occurs the replacement of N=P bond by Cl–P bond, the energy difference of which is considerable smaller.

Trichloroisophosphazoacyls are quite stable in the absence of moisture and may be stored in tightly closed vessels at room temperature for many months without change. They are rapidly hydrolyzed by the action of atmospheric moisture. Hydrolysis of trichloroisophosphazoacyls by means of formic acid proceeds in a more complex manner, in contrast to the analogous reaction of trichlorophosphazoacyls [6], and yields waxy substances the nature of which has not been studied so far. Trichloroisophosphazoacyls react just as energetically with alcohols, water, ammonia, amines, phenols and other substances containing active hydrogen atoms, as do trichlorophosphazoacyls. Therefore, trichloroisophosphazoacyls may serve as the starting materials for the preparation of varied derivatives of phosphoric acid of new types, these being the corresponding derivatives of the reactants listed above.

Several previously undescribed trichlorophosphazoacyls and dichlorides of acylamidophosphoric acids were synthesized for use as starting materials, as were the corresponding acylamidophosphoric acids.

## EXPERIMENTAL

General method of preparation of trichloroisophosphazoacyls [by scheme (3)]. A mixture of 0.05 mole of the dichloride of the appropriate acylamidophosphoric acid and 0.051 mole of powdered phosphorus pentachloride (in case of the tetrachloride of isophthaloylbisamidophosphoric acid there was used 0.102 mole) was heated on an oil bath at 125-135° until hydrogen chloride evolution stopped completely, which required 20-25 minutes. During this time some 85-95% of the theoretical amount of hydrogen chloride was formed. Phosphorus oxychloride was distilled in vacuum. The residue contained trichloroisophosphazoacyls in the form of colorless transparent viscous liquids which on being cooled to −70° were transformed into glassy transparent fragile masses. The yields were almost quantitative. Trichloroisophosphazo-p-nitrobenzoyl [2] and trichloroisophosphazo-3,5-dinitrobenzoyl are crystalline substances.

All the trichloroisophosphazoacyls are rather readily soluble in benzene, more difficultly in carbon tetrachloride and petroleum ether. For analytical data see Table 1.

Thermal decomposition of trichloroisophosphazoacyls [by scheme (4)]. Into a Claisen flask with two thermometers there was charged 0.02 mole of trichloroisophosphazoacyl. The bulb of one thermometer was immersed into the substance while the bulb of the other was in the vapor space. The flask contents were gradually heated on an oil bath. The decomposition proceeds in the interval of 130-200° depending on the nature of the trichloroisophosphazoacyl compound and is terminated in 30-40 minutes. During this interval from 65 to 95% of phosphorus oxychloride distills. In some cases the mixture of the products of decomposition was distilled in vacuum for the complete removal of phosphorus oxychloride.

The yields of the nitriles, after water washing, were almost quantitative. The identification of the nitriles and $POCl_3$ were done by the usual methods.

Preparation of trichlorophosphazoacyls [by scheme (1)]. A mixture of 0.03 mole of an amide of carboxylic acid, 0.031 mole of phosphorus pentachloride and 100 ml of carbon tetrachloride were refluxed until the evolution of hydrogen chloride was complete, which requires 20-25 minutes. Carbon tetrachloride was distilled in vacuum. Trichlorophosphazoacyls remain in the residue; yields – about 100%. The following compounds were obtained in this fashion.

Trichlorophosphazo-p-toluyl, a viscous liquid, which changed to a fragile glassy mass on being chilled to −70°; it is readily soluble in benzene and carbon tetrachloride; difficultly soluble in ether and petroleum ether.

Found %: Cl 38.91; P 11.56. Equivalent after hydrolysis 4.91. $C_8H_7ONPCl_3$. Calculated %: Cl 39.44; P 11.47. Equivalent after hydrolysis 5.00.

Trichlorophosphazo-α-naphthoyl crystallizes from petroleum ether in fused needles, m.p. 66-68°; it is readily soluble in benzene, less readily in carbon tetrachloride, ether, dioxane, and petroleum ether.

Found %: Cl 34.81; P 10.62. Equivalent after hydrolysis 4.98. $C_{11}H_7ONPCl_3$. Calculated %: Cl 34.70; P 10.10. Equivalent after hydrolysis 5.00.

Trichlorophosphazo-β-naphthoyl, a viscous liquid which crystallizes to fused needles on being chilled to −35° to −40°; readily soluble in benzene and carbon tetrachloride, and difficultly soluble in ether and petroleum ether.

Found %: Cl 34.61; P 10.00. Equivalent after hydrolysis 4.93. $C_{11}H_7ONPCl_3$. Calculated %: Cl 34.70; P 10.10. Equivalent after hydrolysis 5.00.

Trichlorophosphazo-2,4-chloronitrobenzoyl, described previously as a light yellow liquid [3], crystallized after shaking with petroleum ether and chilling; m.p. 62-64°; large, almost colorless prisms (from petroleum ether). Readily soluble in benzene and carbon tetrachloride; less readily soluble in ether and petroleum ether.

Found %: hydrolyzable Cl 31.58; P 9.31. Equivalent after hydrolysis 5.02. $C_7H_3O_3N_2PCl_4$. Calculated %: hydrolyzable Cl 31.68; P 9.22. Equivalent after hydrolysis 5.00.

TABLE 1

Trichloroisophosphazoacyls of Type $RCCl=NPOCl_2$

| R | Appearance | Found |  |  | Empirical formula | Calculated* (in %) |  | Thermal decomposition by scheme (4) |  |  |  |
|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  | Cl (%) | P (%) | acid equiv. after hydrol. |  | Cl | P | temp. | time of cleavage (in minutes) | yield of $POCl_3$ (in %) | yield of RNC (in %) |
| $C_6H_5$ | Viscous liquid | 41.00 | 12.11 | 4.97 | $C_7H_5ONPCl_3$ | 41.49 | 12.10 | 210—215° | 30 | 91.4 | 82.4 |
| $p\text{-}CH_3C_6H_4$ | „ „ | 39.75 | 11.45 | 4.87 | $C_8H_7ONPCl_3$ | 39.32 | 11.45 | 200—205 | 25 | 78.4 | 96.4 |
| $\alpha\text{-}C_{10}H_7$ | „ „ | 34.52 | 10.12 | 5.01 | $C_{11}H_7ONPCl_3$ | 34.70 | 10.10 | 135—140 | 10 | 88.6 | 86.4 |
| $\beta\text{-}C_{10}H_7$ | „ „ | 34.31 | 10.26 | 4.91 | $C_{11}H_7ONPCl_3$ | 34.70 | 10.10 | 140—150 | 10 | 65.5 | 91.9 |
| $o\text{-}ClC_6H_4$ | „ „ | 36.76 ** | 10.65 | 4.91 | $C_7H_4ONPCl_4$ | 36.59 ** | 10.65 | 175—185 | 40 | 95.0 | 98.3 |
| $p\text{-}ClC_6H_4$ | „ „ | 36.41 ** | 10.60 | 5.01 | $C_7H_4ONPCl_4$ | 36.59 ** | 10.65 | 210—215 | 35 | 91.5 | 100.0 |
| $2,4\text{-}Cl_2C_6H_3$ | „ „ | 32.61 ** | 9.50 | 4.98 | $C_7H_3ONPCl_5$ | 32.71 ** | 9.52 | 175—180 | 40 | 75.6 | 99.0 |
| $o\text{-}NO_2C_6H_4$ | „ „ | 35.32 | 10.11 | 4.89 | $C_7H_4O_3N_2PCl_3$ | 35.30 | 10.28 | 130—135 | 40 | 86.7 | 100.0 |
| $m\text{-}NO_2C_6H_4$ | „ „ | 35.43 | 10.38 | 5.01 | $C_7H_4O_3N_2PCl_3$ | 35.30 | 10.28 | 180—190 | 80 | 82.6 | 100.0 |
| $p\text{-}NO_2C_6H_4$ | Prisms ***<br>m. p. 121—124° | 35.52 | 10.25 | 4.93 | $C_7H_4O_3N_2PCl_3$ | 35.30 | 10.28 | 215—220 | 40 | 88.4 | 94.5 |
| $3,5\text{-}(NO_2)_2C_6H_3$ | Prisms ****<br>m. p. 82—84° | 30.21 | 8.88 | 4.86 | $C_7H_3O_5N_3PCl_3$ | 30.72 | 8.94 | 180—190 | 20 | 91.6 | 95.8 |
| $2,4\text{-}ClNO_2C_6H_3$ | Viscous liquid | 31.20 ** | 9.25 | 4.91 | $C_7H_3O_3N_2PCl_4$ | 31.68 ** | 9.22 | 170—180 | 15 | 86.7 | 90.1 |
| $m\text{-}C_6H_4(CCl=NPOCl_2)_2$ | „ „ | 49.10 | 14.61 | 10.00 | $C_8H_4O_2N_2P_2Cl_6$ | 48.90 | 14.26 | 135—140 | 10 | 91.6 | 93.9 |

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*For all (except the last compound) the calculated equivalent is 5.00 after hydrolysis, for the last compound it is 10.00.

**Hydrolyzable chlorine;

***Recrystallized from mixture of benzene and petroleum ether.

****Recrystallized from petroleum ether.

Bis-trichlorophosphazoisophthaloyl. A mixture of 0.03 mole of isothalic diamide, 0.062 mole of phosphorus pentachloride and 80 ml of carbon tetrachloride refluxed until the evolution of hydrogen chloride was complete, required 2-2.5 hours for this reaction. Carbon tetrachloride was distilled in vacuum and the solid residue (yield 100%) was recrystallized from petroleum ether. Large colorless prisms, m.p. 96-99°; readily soluble in benzene, somewhat less readily in carbon tetrachloride, difficultly soluble in ether and petroleum ether.

Found %: Cl 48.72; P 14.32. Equivalent after hydrolysis 9.99. $C_8H_4O_2N_2P_2Cl_6$. Calculated %: Cl 48.90; P 14.26. Equivalent after hydrolysis 10.00.

Thermal cleavage of trichlorophosphazoacyls [by scheme (5)] in contrast to the thermal cleavage of trichloroisophosphazoacyls [by scheme (4)] is an exothermic reaction. The substance is placed into a small Claisen flask and is slowly heated on an oil bath. As soon as the decomposition starts, the flask is removed from the oil bath. Even then the temperature of the reaction mixture rises by 10-30° from the heat of reaction. After the temperature ceases to rise, the flask is again immersed in the oil bath and after several minutes the reaction mixture is distilled in vacuum through a small column. The nitriles and phosphorus oxychloride were identified by the usual methods. The yields were almost quantitative. The temperatures of initiation of decomposition are given in Table 2.

TABLE 2

Thermal Decomposition of Trichlorophosphazoacyls of Type RCON : $PCl_3$ According to Scheme (5)

| R | M. p. | Temp. of start of decomp. | R | M. p. | Temp. of start of decomp. |
|---|---|---|---|---|---|
| $C_6H_5$ | 60—61° [3] | 135—136° | o-$NO_2C_6H_4$ | Liquid | 115—120° |
| p-$CH_3C_6H_4$ | Liquid | 120—130 | m-$NO_2C_6H_4$ | 103—105° | 125—130 |
| α-$C_{10}H_7$ | 66—68 | 125—130 | p-$NO_2C_6H_4$ | 121—123 | 125—130 |
| β-$C_{10}H_7$ | —40—35 | 90—100 | 3,5-$(NO_2)_2C_6H_3$ | 125—126 | 135—140 |
| o-$ClC_6H_4$ | Liquid | 100—105 | 2,4-$ClNO_2C_6H_3$ | 62—64 | 100—105 |
| p-$ClC_6H_4$ | 62—63 | 105—110 | $C_6H_4(CON{=}PCl_3)_2$ | 96—99 | 125—130 |
| 2,4-$Cl_2C_6H_3$ | Liquid | 120—125 | | | |

Preparation of dichlorides of acylamidophosphoric acids [by scheme (2)] was run by the previously described general method [6]. All these products were difficultly soluble in benzene and carbon tetrachloride and insoluble in petroleum ether.

Dichloride of p-toluylamidophosphoric acid, yield 93.4%, prisms, m.p. 99-101°.

Found %: Cl 28.00; P 12.23. Equivalent after hydrolysis 3.98. $C_8H_8O_2NPCl_2$. Calculated %: Cl 28.13; P 12.29. Equivalent after hydrolysis 4.00.

Dichloride of α-naphthoylamidophosphoric acid, yield 84.2%; colorless large prisms; m.p. 99-101° (the melt has bright raspberry color).

Found %: Cl 24.70; P 10.81. Equivalent after hydrolysis 4.00. $C_{11}H_8O_2NPCl_2$. Calculated %: Cl 24.61; P 10.75. Equivalent after hydrolysis 4.00.

Dichloride of β-naphthoylamidophosphoric acid, yield 90.7%; prisms; m.p. 111-113°.

Found %: Cl 24.52; P 10.80. Equivalent after hydrolysis 3.96. $C_{11}H_8O_2NPCl_2$. Calculated %: Cl 24.61; P 10.75. Equivalent after hydrolysis 4.00.

Tetrachloride of isophthaloylbis-amidophosphoric acid, yield 95.6%; prisms, m.p. 130-131°.

Found %: Cl 35.41. Equivalent after hydrolysis 8.10. $C_8H_6O_4N_2P_2Cl_4$. Calculated %: Cl 35.62. Equivalent after hydrolysis 8.00.

Acylamidophosphoric acids of type $RCONHPO(OH)_2$ were prepared from the dichlorides of acylamidophosphoric acids by the previously described method [7].

p-Toluylamidophosphoric acid, yield quantitative, crystallizes in plates; m.p. 158-159°; readily soluble in water, acetone and alcohol; difficultly soluble in benzene and carbon tetrachloride.

Found %: P 14.49. Equivalent 1.98. $C_8H_{10}O_4NP$. Calculated %: P 14.40. Equivalent 2.00.

α-Naphthoylamidophosphoric acid, yield almost quantitative; crystallized in prisms; m.p. 139-141°.

Found %: P 12.21. Equivalents 1.98. $C_{11}H_{10}O_4NP$. Calculated %: P 12.33. Equivalents 2.00.

β-Naphthoylamidophosphoric acid, yield quantitative; microcrystalline powder; m.p. 155-157°.

Found %: P 12.30. Equivalents 1.98. $C_{11}H_{10}O_4NP$. Calculated %: P 12.33. Equivalents 2.00.

α- and β-Naphthoylamidophosphoric acids are readily soluble in alcohol, dioxane, acetone; less readily soluble in water; sparingly soluble in benzene and carbon tetrachloride; insoluble in ether and petroleum ether.

We failed to prepare the free isophthaloylbisamidophosphoric acid since in the hydrolysis of its tetrachloride there occurred the cleavage of phosphoric acid and there formed only the diamide of isophthalic acid.

## SUMMARY

The reaction of preparation of trichloroisophosphazoacyls from the dichlorides of acylamidophosphoric acids and phosphorus pentachloride is a general reaction for the aromatic series. Several trichloroisophosphazoacyls of the aromatic series were prepared and their properties were described.

## LITERATURE CITED

[1] A. V. Kirsanov and G. I. Derkach, J. Gen. Chem. 26, 2009 (1956).*

[2] A. V. Kirsanov and G. I. Derkach, J. Gen. Chem. 27, 3248 (1957).*

[3] A. V. Kirsanov, Bull. Acad. Sci. USSR, Ser. Chem. 1954, 646;* A. V. Kirsanov and R. G. Makitra, J. Gen. Chem. 26, 907 (1956).*

[4] A. V. Kirsanov, Bull. Acad. Sci. USSR, Ser. Chem. 1952, 710;* 1954, 646.*

[5] J. V. Braun, Ber. 37, 2814 (1904).

[6] A. V. Kirsanov and R. G. Makitra, J. Gen. Chem. 26, 905 (1956).*

[7] A. V. Kirsanov and R. G. Makitra, J. Gen. Chem. 27, 450 (1957).*

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# BIS-TRIARYLOXYPHOSPHAZO-SULFONES AND TETRAARYL ESTERS OF SULFAMIDOBISPHOSPHORIC ACID

A. V. Kirsanov and L. L. Matveenko

Only bis-trichlorophosphazo-sulfone [1] has been described thus far among the possible derivatives of sulfamidobisphosphoric acid. Neither bis-triaryloxyphosphazo-sulfones nor esters of sulfamidobisphosphoric acids have been known up to the present time.

Bis-trichlorophosphazo-sulfone reacts energetically with phenolates. On mixing dry phenolates with bis-trichlorophosphazo-sulfone the reaction mixture heats up so much that smoke forms and the reaction mixture chars. In the presence of solvents, such as benzene or ether, the reaction proceeds more peacefully with formation of the corresponding bis-triaryloxyphosphazo-sulfones (I) (hexaesters of bis-trihydroxyphosphazosulfone) according to the following scheme:

$$SO_2(N{=}PCl_3)_2 + 6NaOAr \longrightarrow SO_2[N{=}P(OAr)_3]_2 + 6NaCl \qquad (II)$$

The reaction of formation of substances (I) is formally quite analogous to the reaction of formation of triaryloxy- or trialkoxyphosphazosulfonalkyls [2] or -aryls [3] (triesters of trihydroxyphosphazosulfonalkyls and aryls) (III) according to the following scheme:

$$RSO_2N{=}PCl_3 + 3NaOAr \longrightarrow RSO_2N{=}P(OAr)_3 + 3NaCl \qquad (IV)$$

However the realization of reaction (II) turned out to be incomparably more complex and difficult than was the realization of reaction (IV). Single-type substances (III), as a rule, were prepared by the same technique with closely similar yields [2, 3]. It was practically impossible to obtain the single-typed substances (I) by the same technique. In the preparation of substances (III) the purity of the starting materials and the details of the reaction conditions do not have a great significance; however, in the preparation of substances (I) the most insignificant contamination of the initial arylates and the most insignificant changes in the conditions of the reaction lead to a severe decline of the quality of the resulting reaction products, especially true for hexanaphthyl and hexatolyl derivatives. This is mainly explained by the considerably greater reactivity of substances (I) in comparison with substances (III), by the high adsorptional ability of solid substances (I) and, most importantly, by the deep-seated principal difference in the nature of these substances despite their formal resemblance, since (I) are derivatives of sulfamide while (III) are derivatives of amides of aryl- or alkylsulfonic acids (see below). Therefore for each specimen of (I) it was necessary to find special conditions of synthesis and purification and, in some cases, it was necessary to use special methods of preparation and purification of the starting arylates. Compounds (I) of type $SO_2[N{=}P(OAr)_3]_2$, with Ar : $C_6H_5$ (V), o-, m- and p-$CH_3C_6H_4$ (VI, VII, VIII), α- and β-$C_{10}H_7$ (IX) and (X), p-$ClC_6H_4$ (XI) and p-$O_2NC_6H_4$ (XII), were prepared by scheme (II).

All the (I) thus prepared were colorless substances of neutral character. Their structure is proved sufficiently regidly by the almost quantitative yield (with example of V), by the analytical data and by the transformation into tetraesters of N,N'-sulfamidobisphosphoric acid (XIV, see below). Despite the large molecular weight (from 712 to 1012) all (I) crystallize well although some of them do so very slowly. Solubility, melting point and other physical and chemical properties are determined largely by the type of the aryl group which is present in the molecule and these vary from compound to compound within rather wide limits (see experimental section). Substances (I) are quite resistant to dilute aqueous solutions of alkalies. A benzene solution of (VI) or (VII) was shaken constantly for three days with 0.5 N solution of sodium hydroxide after which the reaction mixture stood for two weeks longer. After this treatment (VI) and (VII) were recovered unchanged. On boiling (VI), which had been reduced to a fine powder, with 2N aqueous solution of sodium hydroxide the reaction of hydrolysis does proceed but does so very slowly. The stability of (I) to aqueous solutions of alkalies is evidently mainly explained by their insolubility in water. On boiling substances (I) with 2N aqueous solution of alkalies diluted with two parts of alcohol, the hydrolysis reaction is completed within 20-40 minutes according to the scheme:

$$SO_2[N{=}P(OAr)_3]_2 \xrightarrow[+4NaOH]{} 2NaOAr + 2H_2O + SO_2[NNaPO(OAr)_2]_2 \longrightarrow$$
$$\xrightarrow[+2HCl]{} 2NaCl + SO_2[NHPO(OAr)_2]_2$$

In some cases better results are obtained by hydrolysis with alkalies in pyridine-alcohol solution (see experimental part).

Substances (XIV) of the type $SO_2[NHPO(OAr)_2]_2$ with Ar: $C_6H_5$ (XV), o-, m- and p-$CH_3C_6H_4$ (XVI), XVII and XVIII), α- and β-$C_{10}H_7$ (XIX and XX), p-$ClC_6H_4$ (XXI) and p-$O_2NC_6H_4$ (XXII), were synthesized by the scheme shown above. All the (XIV) thus prepared were microcrystalline substances which melted with decomposition and were insoluble or were but sparingly soluble in water; they were soluble in acetone, alcohol, dioxane, and chloroform. They were insoluble, even on heating, in nonpolar organic solvents: benzene, ether, carbon tetrachloride, petroleum ether and dichloroethane; they displace carbon acid from its salts and titrate with two equivalents of aqueous alkalies (with phenolphthalein). In contrast to diesters of arylsulfonamidophosphoric acids, substances (XIV) are rather readily cleaved at the nitrogen to sulfur bond on being boiled with water and especially readily in aqueous alcohol and alcoholic solutions. This fact is explained by the fact that (XIV) are derivatives of sulfamide which is readily hydrolyzed by water, alkalies and acids, while diesters of arylsulfonamidophosphoric acids are derivatives of arylsulfonamides which saponify only extremely difficultly (compare above). Properties of (XV) were studied in most detail, this substance being obtained in the form of finely crystalline snow-white powder with m.p. 185-187° (with decomposition) after reprecipitation with hydrochloric acid from an alkaline solution. It was impossible to recrystallize any significant amounts of (XV) from either water or alcohol (see above). Only a very small amount may be recrystallized from water (see experimental section). The melting point of (XV), recrystallized from water, is 188-189° (with decomposition). On being boiled with 96% alcohol the substance undergoes a cleavage of the sulfur—nitrogen bond and forms the diphenyl ester of amidophosphoric acid (XXV), which was identified by mixed melting point with authentic (XXV) [4], and a mixture of acidic uncrystallizable substances which are readily soluble in water, which were evidently sulfamic acid and diphenyl phosphate

$$[(C_6H_5O)_2PONH]_2SO_2 \xrightarrow[+2H_2O]{} (C_6H_5O)_2PONH_2 + NH_2SO_2OH + (C_6H_5O)_2POOH$$

Substances (XV) form readily crystallizable salts with alkalies: there were prepared sodium, potassium and ammonium salts (see the experimental section).

In their physical and chemical properties (XVI-XVIII) are rather similar to (XV) but in contrast with salts of (XV), the salts of (XVI-XVIII) precipitate from hot aqueous solutions on cooling in the form of an oil which is saturated with water. After being dried in a vacuum desiccator over sulfuric acid these salts gradually lose the water contained in them and are transformed into a hard glassy mass.

We failed to prepare (XIX) by hydrolysis of (IX) with aqueous alcoholic and alcoholic alkali in any satisfactory yield. After many hours of refluxing of the reaction mixture the yield of (XIX) was about 4%. We succeeded in carrying out the hydrolysis of (IX) with good yield in pyridine-alcohol solution (see experimental section).

Substance (XXI) has an interesting peculiarity: when dry it is absolutely in ether, but after being moistened with water it dissolves in ether quite easily. For other properties and peculiarities of (XIV) see the experimental section.

## EXPERIMENTAL

The success of the synthesis of bis-triaryloxyphosphazo-sulfones depends to a considerable degree on the quality of the sodium arylates used for the reaction; these must be finely powdered, thoroughly dried and be quite pure. Thus, for example, after using some insufficiently pure sodium cresolates it was impossible to isolate crystalline forms of (VII) and (VIII). The concentrated aqueous solutions of sodium arylates must be completely colorless or only slightly colored. Solutions of cresolates oxidize especially easily in the presence of excess of the cresols; such solutions darken in the presence of air very rapidly indeed even at room temperature. Therefore, sodium cresolates should be prepared by addition of cresols to precisely equivalent amounts of 20-25% solutions of sodium hydroxide, and not in reverse. The solutions of sodium cresolates should be evaporated in vacuum without a capillary or in a stream of an inert gas, at the temperature of a boiling water bath, with a subsequent drying at 150-180° over 2-3 hours. Both during the evaporation and during drying, right up to final cooling, no contact of the solutions or the solid sodium cresolates with atmospheric oxygen can be permitted. Pure dry cresolates are oxidized by atmospheric oxygen very slowly, but they must be meticulously protected from the action of moisture and carbon dioxide from the atmosphere, since the cresolates are easily oxidized in the presence of these substances.

The products of oxidation of the p-chlorophenolate are not colored, in contrast to the products of oxidation of sodium cresolates. Therefore, the color of the p-chlorophenolate is not a criterion of its purity. A known, spoiled p-chlorophenolate may be completely colorless. The p-chlorophenolate is oxidized by atmospheric oxygen particularly readily in the presence of free p-chlorophenol. In the synthesis of the p-chlorophenolate one may use a slight excess of the alkali, from which the product is easily separated by solution in ether with a subsequent distillation of the solvent in vacuum. About 11 g of sodium p-chlorophenolates dissolves in 100 g of ether. The p-chlorophenolate must be dried in vacuum at a temperature not under 150° and air should be admitted into the flask (nitrogen is better) only after complete cooling. Pure sodium p-chlorophenolate is completely soluble in ether.

Using sodium naphtholates, prepared by the usual method from the naphthols and aqueous solution of sodium hydroxide, it is impossible to prepare in a satisfactory yield the colorless crystalline specimens of (IX) and (X), since sodium naphtholates, either in dry state or in aqueous or ethereal solutions, are extremely easily oxidized by oxygen of the air. Therefore sodium naphtholates must be prepared from naphthols and metallic sodium in ethereal solutions in special apparatus which completely prevents any contact of the ethereal solutions of the naphtholates with oxygen in the air. The reaction of sodium naphtholates with bis-trichlorophosphazo-sulfone was run in the same apparatus in an atmosphere of hydrogen. The preparation and drying of the p-nitrophenolate does not present any difficulties.

All solvents used for the synthesis and the recrystallization of bis-triaryloxyphosphazo-sulfones must be pure and thoroughly dehydrated. All operations must be run in such a manner that the starting materials and the reaction mixtures come in contact with atmospheric moisture as little as possible.

Bis-triphenoxyphosphazo-sulfone (V). To a solution of 0.05 mole of bis-trichlorophosphazo-sulfone (XIII) in 200 ml of benzene there was added at once with energetic stirring 0.31 mole of sodium phenolate which operation causes a vigorous boiling of the mixture. After the cessation of the spontaneous boiling, the mixture was refluxed for thirty minutes on a water bath. The precipitate of sodium phenoxide disappears and there is formed a slimy precipitate of sodium chloride. If the starting materials were pure, the mixture remains quite colorless. The benzene is removed completely in vacuum, finally on a boiling water bath, and 50.0 ml of water is added to the residue, whereupon (V) precipitates in the form of a colorless finely crystalline precipitate. The product is filtered off by suction (the filtrate should be neutral or slightly alkaline but never acidic), washed with water and dried over sulfuric acid in vacuum; yield is 95-98%, m.p. 131-132°. In case the product is obtained in a colored state (this takes place after use of insufficiently pure sodium phenolate) it is washed several times with alcohol, which somewhat reduces the yield. After recrystallization from benzene (16.4 g from 200 ml) there is formed 12.2 g of (V) in the form of colorless flat rectangular prisms with m.p. 132-133°. The substance is insoluble in water and cold petroleum ether; it is soluble with difficulty in boiling petroleum ether, and is readily soluble in boiling alcohol, benzene, carbon tetrachloride, acetone and chloroform, and difficultly soluble in these solvents in the cold. About hydrolysis of (V) see below.

Found %: C 60.43; H 4.19; N 3.77, 3.88; S 4.45; P 8.75. M 695, 705. $C_{36}H_{30}O_8N_2SP_2$. Calculated %: C 60.64; H 4.21; N 3.93; S 4.50; P 8.71. M 712.4.

Bis-tri-o-cresoxyphosphazo-sulfone (VI) was prepared similarly to (V); yield 93-95%. Soluble in all organic solvents considerably more readily than (V). Crystallizes from benzene with one molecule of benzene, the crystallohydrate having m.p. 105-115°.

Found %: $C_6H_6$ 9.22. $C_{42}H_{42}O_8N_2SP_2 \cdot C_6H_6$. Calculated %: $C_6H_6$ 9.81.

The crystallohydrate with benzene is easily "weathered" in air or by washing with ether. After drying in vacuum at 100° or crystallization from ether there is obtained (VII) which does not contain the benzene of crystallization; m.p. 127-129°.

Found %: N 3.42, 3.34. $C_{42}H_{42}O_8N_2SP_2$. Calculated %: N 3.52.

Bis-tri-m-cresoxyphosphazo-sulfone (VII). The synthesis was run as was that of (V). After distillation of benzene in vacuum there remained a viscous uncrystallizing mixture of sodium chloride and (VII) to which there was added 200-250 ml of ether (free of peroxides) and 100 ml of water and the mixture was shaken energetically. After separation of the aqueous layer, the ethereal layer was washed with N solution of sodium hydroxide and several times with 10-15% solution of sodium chloride. If the ethereal layer remained cloudy, it was finally washed with a saturated solution of sodium chloride. The ethereal solution was washed as above, then dried with sodium sulfate, after which the ether was distilled, finally in vacuum. The residue was crude (VII) in the form of a viscous almost colorless slowly crystallizing oil. The composition of the crude (VII) in respect to nitrogen content did not differ from that of pure crystalline substance; the yield was about 90%. For preparation of the crystalline substance, there was added to crude (VII) such a volume of ether so as to bring the entire mass into solution on heating, after which the solution was filtered if needed, and was treated with petroleum ether (85-95°) in the amount needed to cause cloudiness. A crystalline seed was added to the solution and this was allowed to stand for one day at room temperature. Large well formed prismatic crystals of (VII) precipitated from the solution; yield was about 40%; m.p. 54-56°.

Found %: N 3.52. $C_{42}H_{42}O_8N_2SP_2$. Calculated %: N 3.52.

Bis-tri-p-cresoxyphosphazo-sulfone (VIII) was prepared just like (VII), but crystallized much more readily. The yield of crude (VIII) in the form of oil was 88.0%; the yield of crystalline (VIII) was 62.0%; m.p. 80-81°. The compositions of the crude and the crystalline (VIII) in respect to nitrogen content were identical.

Found %: N 3.60. $C_{42}H_{42}O_8N_2SP_2$. Calculated %: N 3.52.

Bis-tri-α-naphthoxyphosphazo-sulfone (IX). The preparation of sodium α-naphtholate, filtration of its solution, its mixing with the solution of (XIII) and the addition of dilute hydrochloric acid to the reaction mixture were all performed in nitrogen atmosphere or hydrogen atmosphere in a special apparatus which permitted the complete prevention of contact by the solutions with atmospheric oxygen. The construction of the apparatus is not described here since it is rather complicated, but this has no fundamental significance. Any apparatus may be suitable as long as it permits one to run the reaction in the absence of atmospheric oxygen.

The filtered solution of 0.066 mole of α-naphthol in 30.0 ml of ether was poured into the flask containing 0.09 gram atoms of sodium in the form of a thin wire (or cut into thin slices) and 25.0 ml of ether. A vigorous reaction began immediately, the solution first turning blue, then soon becoming almost colorless. If necessary, the flask was cooled with cold water. One should watch that the volume of the solution never drops below 45-50 ml owing to the loss of ether by the evolving hydrogen, and one should add small volumes of ether from time to time since the omission of this may result in solid naphtholate depositing on the surface of sodium and thus causing the reaction to stop. After the reaction had been completed, the naphtholate solution was filtered from excess sodium, heated to 30° and added slowly with energetic stirring to the solution of 0.01 mole of (XIII) in 50.0 ml of ether at such a rate as to cause the reaction mixture to boil vigorously. A snow white precipitate forms during this operation, this being a mixture of sodium chloride and (IX). After the vigorous reaction had been completed, the reaction mixture was refluxed for 15-20 minutes on a water bath, then cooled and slowly treated with stirring with 15.0 ml of N hydrochloric acid. The ethereal and the aqueous layers separate rapidly, both being transparent. All further operations were done conventionally. (IX) is present in the aqueous layer in the form of finely crystalline powder which was filtered off, washed thoroughly with ether and water and then dried in air. (IX) prepared in this manner is a completely colorless finely crystalline powder; the yield is 90-95%, after recrystallization from chlorobenzene (5.0 g per 30.0 ml) m.p. 205-206°. If air enters the apparatus during the synthesis prior to the addition of hydrochloric acid, (IX) is obtained in a colored state – from light grey to black. The substance is readily soluble in acetone, difficultly soluble in most of the common organic solvents and insoluble in water.

Found %: N 2.77. $C_{60}H_{42}O_8N_2SP_2$. Calculated %: N 2.76.

Bis-tri-β-naphthoxyphosphazo-sulfone (X) was prepared just like (IX); the yield was 74-79%. For recrystallization, 15.0 g of the product was dissolved in 80.0 ml of acetone; the solution was filtered and somewhat over half of the acetone was distilled off; to the residual solution was added about 100 ml of ether (until cloudiness formed). After one day the precipitated crystals were filtered off by suction and washed with ether; m.p. 133-134°. (X) is readily soluble in acetone, insoluble in water and difficultly soluble in the majority of common organic solvents.

Found %: N 2.85. $C_{60}H_{42}O_8N_2SP_2$. Calculated %: N 2.76.

Bis-tri-p-chlorophenoxyphosphazo-sulfone (XI). To the solution of 0.01 mole of (XIII) in 50.0 ml of ether there was added at once the solution of 0.063 mole of sodium p-chlorophenolate (see above for the preparation of the arylates of sodium) in 100 ml of ether. After the vigorous reaction had subsided (boiling-up, formation of the precipitate), the mixture was refluxed for 20 minutes. Then ether was distilled off in vacuum and 20.0 ml of water was added to the residue. If the starting materials were quite pure, (XI) precipitates in a crystalline form or in the form of an oil which rapidly crystallizes. The product was filtered off, washed with water, 0.2 N solution of sodium hydroxide, then again with water and then dried. The yield was 80-85%. For purification the product was dissolved in 15.0 ml of boiling benzene and then treated with 20-30 ml of petroleum ether. (XI) precipitated from the solution in the form of fine colorless prisms, m.p. 111-113°. It is readily soluble in acetone, difficultly in ether and benzene.

Found %: N 3.16. $C_{36}H_{24}O_8N_2Cl_6SP_2$. Calculated %: N 3.05.

Synthesis of (XI) may be carried out in benzene with dry sodium p-chlorophenolate but the yield in this case is considerably lower. In some cases during the synthesis of (XI) with insufficiently pure dry sodium p-chlorophenolate there were obtained large colorless prisms with m.p. 85-86°, which after recrystallization from ether were converted into pure (XI) with m.p. 111-113°. The mixed melting point of these prisms with (XI) melted at 68-110°. Evidently the substance with m.p. 85-86° was a double complex of (XI) with p-chlorophenol. This substance was not examined in more detail.

Bis-tri-p-nitrophenoxyphosphazo-sulfone (XII). To 0.062 mole of dry powdered sodium p-nitrophenolate there was added with stirring the solution of 0.01 mole (XIII) in 30.0 ml of nitrobenzene. The mixture heated up considerably but failed to boil. After termination of this reaction, the mixture was heated on an oil bath until the p-nitrophenolate dissolved (120-125°). Sodium chloride precipitated on cooling and (XII) began to crystallize in small shiny prisms. To the still warm mixture there was added 50.0 ml of ether, the whole being well stirred, then allowed to stand for two hours, treated with 30.0 ml of water, again stirred vigorously, after which (XII) was filtered off, washed thoroughly with water, then with acetone (twice with 15.0 ml) and ether (three times with 20.0 ml). The yield was 80%. For purification the substance was dissolved in nitrobenzene preheated almost to boiling (1.0 g for 2.0 ml), the solution was immediately filtered while hot, and treated with 5 volumes of acetone. After a few minutes (XII) began to precipitate in the form of small shiny prisms. After one hour the product was filtered off, washed with acetone (five times with 10.0 ml) and ether (four times with 10.0 ml). The yield was 53%; m.p. 198-200°, with sintering noted at 195°.

Found %: N 11.67. $C_{36}H_{24}O_{20}N_8SP_2$. Calculated %: N 11.40.

(XII) may also be prepared in a benzene solution but the yields in this case are low, the reaction must be run for several hours and the isolation of a pure product is complicated by considerable difficulties [see preparation of (V)]. The substance is insoluble in water and the usual organic solvents. It is readily soluble in hot pyridine and nitrobenzene. It decomposes rather rapidly in boiling nitrobenzene solutions.

Tetraphenyl ester of N,N'-sulfamidobisphosphoric acid (XV). To 60.0 ml of 2 N aqueous solution of sodium hydroxide there was added 70.0 ml of alcohol and 0.031 mole of thoroughly powdered (V). The mixture was refluxed with stirring until the precipitate dissolved almost completely, which required about 20 minutes. The solution was filtered and concentrated in vacuum to half the original volume and the residue was treated with a mixture of 25.0 ml of 5 N hydrochloric acid and 20.0 ml of alcohol. Thereby (XV) precipitated in the form of a colorless cheesy mass. The product was filtered off, washed with water and dried in air. The yield was 92.0%. For purification the substance was dissolved in 2 N aqueous alcoholic solution of sodium carbonate and this solution was poured into an aqueous alcoholic solution of 3 N hydrochloric acid. The (XV) prepared in this manner was a colorless finely crystalline powder, m.p. 185-187° (decomposition). On being boiled with water and alcohol the substance decomposes rather rapidly but small amounts of it may be recrystallized from water. To do this one adds 1.0 g of finely powdered (XV) to 300 ml of boiling water, the mixture being shaken vigorously and filtered immediately. On cooling the solution precipitates (XV) in the form of fine shiny needles with m.p. 188-189° (decomposition). See above about the solubility of (XV).

Found %: N 4.83, 4.86. Equivalents 2.01, 2.00. $C_{24}H_{22}O_8N_2SP_2$. Calculated %: N 5.00. Equivalents 2.00.

Cleavage of (XV) on boiling with alcohol. A mixture of 0.01 mole of (XV) and 40.0 ml of 96% ethyl alcohol was refluxed for thirty minutes after which the alcohol was distilled off in vacuum from a water bath. On cooling a crystalline diphenyl ester of amidophosphoric acid (XXV) precipitated, this being filtered off and washed with alcohol (three times with 1.0 ml); m.p. 148-149°; yield 0.0075 mole; the identification was done by mixed melting point with authentic (XXV) [4]. Substances which remained in solution gave an acid reaction with Congo red and decomposed sodium bicarbonate. From 0.01 mole of (XV) there was formed 0.0081 mole of (XXV) and a mobile colorless oil with an acid reaction to Congo red, after an analogous experiment with anhydrous methyl alcohol. Triaryloxyphosphazosulfonophenyls are unchanged even after prolonged boiling with alcohol.

Sodium salt of (XV). (XV) (0.004 mole) was mixed with 5.0 ml of water and 0.004 mole of sodium carbonate. The substance dissolved with hissing. The sodium salt of (XV) precipitated in the form of well developed elongated prisms which were filtered off and washed with a small volume of water. The yield was about 2.2 g; m.p. 44-57°. The salt contains ten molecules of water of crystallization, a considerable part of which is easily lost by simple storage in air, which fact explains the extended melting range.

Found %: $H_2O$ 25.05. $C_{24}H_{20}O_8N_2SP_2Na_2 \cdot 10H_2O$. Calculated %: $H_2O$ 24.69.

The hydrate is completely dehydrated after storage in vacuum over sulfuric acid. The anhydrous salt melts at 252-254° (with decomposition).

Found %: N 4.57. $C_{24}H_{20}O_8N_2SP_2Na_2$. Calculated %: N 4.65.

Decomposition evidently precedes the melting of the anhydrous salt since the salt heated in vacuum above 100° no longer dissolves completely in water and does not regenerate the hydrate on being treated with water, while the salt which had been dried in vacuum over sulfuric acid at room temperature is completely soluble in water and readily regenerates the hydrate with ten molecules of water.

Potassium salt of (XV) was prepared analogously to the sodium salt. The hydrate of the potassium salt contains seven molecules of water of crystallization and melts at 52-54°; it loses water somewhat less readily than does the hydrate of the sodium salt, but it still weathers on being stored in air.

Found %: $H_2O$ 15.90. $C_{24}H_{20}O_8N_2SP_2K_2 \cdot 7H_2O$. Calculated %: $H_2O$ 16.53.

The hydrate loses water completely in vacuum at 40-50°.

Found %: N 4.46. $C_{24}H_{20}O_8N_2SP_2K_2$. Calculated %: N 4.40.

Ammonium salt of (XV). (XV) (0.002 mole) was dissolved with mild heating in 2.0 ml of concentrated aqueous solution of ammonia. Small colorless crystals of the ammonium salt precipitated on cooling; yield was 1.22 g; m.p. 63-67°. The salt contained four molecules of water of crystallization which were not weathered off in storage in air.

Found %: $H_2O$ 10.92. $C_{24}H_{28}O_8N_4SP_2 \cdot 4H_2O$. Calculated %: $H_2O$ 10.81.

The hydrate loses water completely in vacuum at 100°.

Found %: N 8.45. $C_{24}H_{28}O_8N_4SP_2$. Calculated %: N 8.45.

Tetra-o-tolyl ester of sulfamidobisphosphoric acid (XVI) was prepared just like (XV). Yield was 80%; m.p. 173-176° (with decomposition).

Found %: N 4.37. Equivalents 1.97. $C_{28}H_{30}O_8N_2SP_2$. Calculated %: N 4.55. Equivalents 2.00.

Tetra-m-tolyl ester of sulfamidobisphosphoric acid (XVII) was prepared just like (XV) but refluxing was continued for one hour since (VII) hydrolyzes considerably more slowly than does (V). The yield was 73%; m.p. 170-172° (with decomposition).

Found %: N 4.56. Equivalents 2.00. $C_{28}H_{30}O_8N_2SP_2$. Calculated %: N 4.55. Equivalents 2.00.

Tetra-p-tolyl ester of sulfamidobisphosphoric acid (XVIII) was prepared just like (XVII). Yield was 87%; m.p. 184-185° (with decomposition).

Found %: N 4.36. Equivalents 2.00. $C_{28}H_{30}O_8N_2SP_2$. Calculated %: N 4.55. Equivalents 2.00.

Tetra-α-naphthyl ester of sulfamidobisphosphoric acid (XIX). To 16.0 ml of N alcoholic solution of potassium hydroxide there was added a hot solution of 0.004 mole (IX) in 10.0 ml pyridine and the mixture was refluxed. It was impossible to determine the end of the reaction by dilution of a sample with water since the potassium salt of (XIX) is very difficultly soluble in water and precipitates on dilution along with unreacted (IX). Under the above conditions the hydrolysis is completed during 1-1.5 hours. The solution was filtered while hot and to the filtrate there was added with stirring 15.0 ml of concentrated hydrochloric acid. (IX) was filtered off after one day; it was washed thoroughly with water then with ether. The yield was 92%. For purification (XIX) was dissolved in 0.3 N alcoholic potassium hydroxide and the hot solution was treated with hydrochloric acid. (XIX) precipitated on cooling in the form of small shiny crystals; m.p. 213-215° (with decomposition).

Found %: N 3.78. Equivalents 2.02. $C_{40}H_{30}O_8N_2SP_2$. Calculated %: N 3.68. Equivalents 2.00.

(XIX) decomposes considerably more slowly than does (XV)-(XVIII) on being boiled in aqueous alcoholic solutions. Sodium salt of (XIX) is more difficultly soluble in water and for this reason the titrations are run in hot aqueous alcoholic solution.

Tetra-β-naphthyl ester of sulfamidobisphosphoric acid (XX). A mixture of 0.004 mole of finely powdered (X), 8.2 ml of 2 N potassium hydroxide and 25.0 ml of alcohol were refluxed until the substance had dissolved completely (30-40 minutes), when a mixture of 5.0 ml of 5 N hydrochloric acid and 5.0 ml of alcohol was added. (XX) was filtered off after several hours and was thoroughly washed with water and ether to remove traces of naphthol. The yield was 94%. From dilute hot aqueous alcoholic solution one may precipitate (XX) by acidification; it forms fine shiny prisms; m.p. 195-198° (with decomposition). (XX) is titrated just like (XIX).

Found %: N 3.70. Equivalents 1.97, 2.01. $C_{40}H_{30}O_8N_2SP_2$. Calculated %: N 3.68. Equivalents 2.00.

Tetra-p-chlorophenyl ester of sulfamidobisphosphoric acid (XXI). A mixture of 0.002 mole (XI), 4.0 ml of 2 N potassium hydroxide and 8.0 ml of alcohol were refluxed until the substance dissolved completely (10-15 minutes), after which there was added 2.0 ml of 5 N hydrochloric acid. The solution at first turned cloudy and after several minutes there began to precipitate the thread-like crystals. (XXI) was filtered off after one day and was washed with water. The yield was 79%; m.p. 183-185° (with decomposition).

Found %: N 4.03. Equivalents 2.01. $C_{24}H_{18}O_8N_2Cl_4SP_2$. Calculated %: N 4.02. Equivalents 2.00.

Tetra-p-nitrophenyl ester of sulfamidobisphosphoric acid (XXII). (XII) (0.02 mole) was refluxed with 8.0 ml of N alcoholic solution of potassium hydroxide and 17.0 ml of alcohol until the precipitate was completely dissolved (30-40 minutes). The cloudy yellow solution was filtered hot and after cooling was treated with 5.0 ml of 2 N hydrochloric acid. (XXII) precipitated in the form of a very fine crystalline powder which was filtered off and washed with a large volume of water, followed by ether. The yield was about 30%. Salts of (XXII) are very difficultly soluble in water and alcohol, which fact complicates the purification of (XXII). The substance decomposes rapidly on being heated in alcoholic or aqueous solutions. It is best to reprecipitate (XXII) from hot solutions in 0.1 N alcoholic potassium hydroxide. The reprecipitated (XXII) forms a finely crystalline powder; m.p. 218-221°.

Found %: N 11.38. $C_{24}H_{18}O_{16}N_6SP_2$. Calculated %: N 11.35.

## SUMMARY

The reaction of bis-trichlorophosphazo-sulfone with sodium arylates was studied and bis-triaryloxyphosphazo-sulfones were prepared.

The hydrolysis of bis-triaryloxyphosphazo-sulfones was studied and tetraaryl esters of sulfamidobisphosphoric acid were prepared.

## LITERATURE CITED

[1] A. V. Kirsanov, J. Gen. Chem. 22, 2346 (1952).*

[2] A. V. Kirsanov and N. L. Egorova, J. Gen. Chem. 28, 1052 (1958).*

[3] A. V. Kirsanov and V. I. Shevchenko, J. Gen. Chem. 24, 474, 882, 1980 (1954).*

[4] L. Audrieth and A. Toy, J. Am. Chem. Soc. 63, 2117 (1947).

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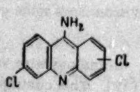
# CHEMICAL STRUCTURE AND PARASITOCIDAL ACTIVITY

## XXI. CONCERNING THE PROBLEM OF THE CONNECTION OF THE STRUCTURAL STABILITY OF DERIVATIVES OF 9-AMINOACRIDINE AND THEIR ANTIMALARIAL ACTION

A. F. Bekhli

The acridine nucleus and the dialkylaminoalkylamine side chain in 9-position are the basic structural elements of the most important group of antimalarial compounds – derivatives of 9-aminoacridine. Various points of view have been expressed about the mechanism of action of these compounds against the plasmodiae. On one hand, attempts were made to explain the activity by the action of the products of decomposition of derivatives of 9-aminoacridine on the parasite [1]; on the other hand, the activity was explained by the action of the whole, intact molecule [2-4]. We set for our goal the study of the dependence of antimalarial action on the stability of the fundamental structure of the molecule, i.e., on the relative stability of the link of the side chain with the acridine nucleus. It was established by biological tests in the groups of monochloro- and dichloro isomers of 9-dialkylamino-alkylaminoacridine [5, 6] synthesized by us, that the degree of the antimalarial activity is connected with the position of the halogen in the acridine nucleus. The determination of the rate of hydrolytic cleavage of ammonia from the group of monochloro isomers of 9-aminoacridine, performed by us [7], showed that the largest amount of ammonia is cleaved from 4-chloro-9-aminoacridine, whose dialkylaminoalkyl analog is inactive against malaria. Conversely, a considerable structural stability under hydrolytic conditions was shown by 1- and 3-chloro derivatives of 9-aminoacridine, whose 9-dialkylaminoalkyl analogs were the most effective agents against malaria.

The purpose of the present work is the further study of the dependence of the antimalarial activity on the hydrolyzability in the series of dichloro derivatives of acridine. In view of the fact that 9-aminoacridines are close to N-monosubstituted derivatives of 9-aminoacridines [8] in their chemical and physical properties and considering that the hydrolysis of 9-aminoacridines may be controlled more readily, we took for our study in this case, as well, the analogs of dichloro isomers of 9-dialkylaminoalkylaminoacridines which did not contain alkyl groups, for the study of the rate of hydrolysis of these substances. For this we synthesized 1,6-, 2,6-, 3,6-, and 4,6-dichloro derivatives of 9-aminoacridine and subjected them to alkaline hydrolysis. These compounds were prepared by condensation of the corresponding 9-phenoxy compounds with ammonium chloride [9] or of the corresponding 9-chloro derivatives with ammonium carbonate [10] in phenol. The hydrolysis was run in a basic solution with titration of the evolved ammonia by the method which has been described previously by us [7]. At the same time we showed that the rate of hydrolysis was the same in acidic and basic media. The results of the hydrolysis are shown in Table 2.



The data secured by us indicate that the least stable, under the conditions of the hydrolysis, is 4,6-dichloro-9-aminoacridine, whose dialkylaminoalkyl analog turned out to be completely inactive against malaria. The other isomers possess greater stability to hydrolytic cleavage, losing a smaller amount of ammonia. At the same time it was found that their dialkylaminoalkyl analogs possess antimalarial activity.

It should be mentioned that the technique used by us brings out in this group of compounds only the basic character of the dependence of the relative stability of the molecule to hydrolysis, their antimalarial activity and the position of the halogen. This dependence shows that one of the necessary conditions for antimalarial activity

TABLE 1

Dichloro-9-aminoacridines

| Position of chlorine atoms | Method | Melting point* | Yield (in %) | Found N** (in %) |
|---|---|---|---|---|
| 1,6- | B | 265—266° | 40 | 10.33, 10.76 |
| 2,6- | B | 299—300 | 40 | 10.61, 10.56 |
| 3,6- | B | 293—294 | 37.9 | 10.73, 10.48 |
| 4,6- | A | 271—272 | 91.2 | 10.57, 10.79 |

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*The compounds were crystallized from alcohol.

**$C_{13}H_8N_2Cl_2$. Calculated %: N 10.65.

TABLE 2

| Position of chlorine atoms in dichloro-9-aminoacridine | Sample (in g) | Amount of 0.01 N HCl consumed in neutralization of ammonia distilled with 100, 150 and 200 ml of water | | |
|---|---|---|---|---|
| | | 100 | 150 | 200 |
| 1,6- | 0.1020 | 6.8 | 7.9 | 9.0 |
| | 0.1018 | 6.4 | 7.2 | 8.0 |
| | 0.1019 | 6.5 | 7.7 | 8.4 |
| 2,6- | 0.1018 | 4.6 | 5.4 | 6.4 |
| | 0.1018 | 5.2 | 6.3 | 7.2 |
| | 0.1019 | 4.3 | 5.0 | 5.5 |
| 3,6- | 0.1018 | 6.3 | 7.2 | 7.9 |
| | 0.1020 | 6.9 | 7.8 | 8.8 |
| | 0.1018 | 6.3 | 7.7 | 8.8 |
| 4,6- | 0.1027 | 9.0 | 11.0 | 12.5 |
| | 0.1018 | 8.0 | 10.1 | 11.4 |
| | 0.1018 | 8.0 | 9.4 | 10.9 |

in this group of compounds is the structural stability of the molecule. Thus, with a few and thus far unexplained exceptions (for example: 2,6-dichloro-9-aminoacridine), the considerable resistance to hydrolytic cleavage is observed in the most active compounds of the series. The establishment of more precise interrelationships between hydrolyzability and antimalarial activity of the compounds is hindered by the insufficient accuracy of the analytical methods used and possible variations of the results of the biological tests. The above conclusion finds some confirmation in the examination of some experimental data obtained by other investigators.

We compared the data on the determination of the rate of hydrolysis among atebrin homologs with various lengths of the side chain [11], with their antimalarial activity found by other investigators [12]. This contraposition showed that the rate of hydrolysis decreases with the increase of antimalarial activity in the groups of 9-dialkylaminoalkylacridines themselves. The synthesized 2-methoxy-6-chloro-7-amino-9(δ-diethylamino-α-methylbutyl)aminoacridine [13-15] and some of its analogs, which have high chemotherapeutic indexes than does acriquine show at the same time a greater stability than the latter on being boiled with water and in a weakly acidic solution. Finally we should note the facile hydrolyzability of the acridine derivatives with a tertiary nitrogen atom in 9-position [1, 16, 17] and should compare it with the absence of any antimalarial effectiveness of such compounds, as for example the N-formyl derivative of atebrin [18].

Thus, this group of compounds also confirms that the derivatives of 9-aminoacridine which are ineffective against malaria are simultaneously unstable to hydrolysis. At the same time, compounds which are stable under the conditions of hydrolysis show a high antimalarial activity. Regardless of the factors which may affect the stability of the link of the acridine nucleus with the side chain, the presence of such a stability is one of the conditions for antimalarial activity of derivatives of 9-aminoacridine.

## EXPERIMENTAL

Dichloro-9-aminoacridines were prepared by the method of Drozdov [9] (method A) by condensation of 9-phenoxy derivatives of acridine with ammonium chloride in phenol, and by the method of Albert [10] (method B) by the reaction of appropriate derivatives of 9-chloroacridine with ammonium carbonate, in phenol. The substances prepared by us are given in Table 1.

The determination of the relative rates of hydrolysis of dichloro-9-aminoacridines was performed by the method described by us previously [7] for the hydrolysis of monochloro-9-aminoacridines in a basic medium with absorption of the ammonia. The experimental conditions were the same for all the compounds studied. The results which were secured are shown in Table 2.

## SUMMARY

1. Isomeric 1,6-, 2,6-, 3,6-, and 4,6-dichloro-9-aminoacridines were synthesized.

2. The relative rates of hydrolysis of the synthesized isomeric dichloro-9-aminoacridines were determined by their being boiled in a basic medium. It was found that the compounds being studied lost ammonia at different rates; the greatest rate of decomposition was discovered in 4,6-dichloro isomer.

3. The closeness of the chemical properties of the dichloro-9-aminoacridines studied by us to those of the corresponding dichloro-9-dialkylaminoalkylaminoacridines permits us to characterize the relative stability of the link of the nucleus with the side chain among the latter group of compounds, on the basis of the data secured about the hydrolysis of the former group. The results which were obtained showed, in comparison with the data from other authors, that the antimalarial action of the dichloro derivatives of 9-dialkylaminoalkylaminoacridine is possible only under the condition of a sufficient stability of these compounds to hydrolytic decomposition; this gives us the basis to regard the antimalarial action as being manifested by the intact unchanged molecule.

## LITERATURE CITED

[1] O. Iu. Magidson and A. M. Grigorovskii , J. Gen. Chem. 6, 806 (1936).

[2] R. J. Hewitt and A.P. Richardson, J. Inf. Dis. 73, 1 (1943).

[3] E. K. Marshall and J. H. Dearborn, J. Pharm. Exp. Ther. 88, 142 (1946).

[4] E. Bock and M. Oesterlin, Zentr. Bakt. Parasitenk. I. Abt. Orig. 143, 306 (1939); C . A. 36, 6665 (1942).

[5] K. S. Topchiev and A. F. Bekhli, Doklady Akad. Nauk SSSR 55, 635 (1947).

[6] A. F. Bekhli, J. Gen. Chem. 23, 329 (1953).*

[7] K. S. Topchiev, A. F. Bekhli and M. L. Kirmalova, J. Gen. Chem. 19, 561 (1949). *

[8] M. A. Acheson, Acridine, N.Y.-London, 90 (1956).

[9] N. S. Drozdov and O. M. Cherntsov, J. Gen. Chem. 5, 1736 (1935).

[10] Syntheses of Organic Preparations, Vol. 3, 36 (1952; Moscow).**

[11] D. L. Hammick, S. F. Mason and L. W. Meacock, J. Chem. Soc. 1952, 4745.

[12] F. J. Wiselog, A survey of Antimalarial Drugs, II, 2 (1946).

[13] A. M. Grigorovskii and E. M. Terent'eva, J. Gen. Chem. 27, 517 (1957).*

[14] A. M. Grigorovskii and T. A. Veselitskaia, J. Gen. Chem. 26, 466 (1956).*

[15] A. M. Grigorovskii, Dissertation "Studies in the Field of Atebrin Derivatives," Moscow; p. 165 (1951).**

[16] A. Albert and B. Ritchie, J. Chem. Soc. 1943, 458.

[17] W. Goodall and Kermack, J. Chem. Soc. 1939, 1546.

[18] F. Schönhöfer, Z. Physiol. Chem. 271, 1 (1942).

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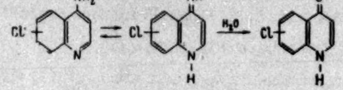
# CHEMICAL STRUCTURE AND PARASITOCIDAL ACTIVITY

## XXII. CONCERNING THE PROBLEM OF THE CONNECTION BETWEEN THE STRUCTURE AND THE ANTIMALARIAL ACTION OF ISOMERIC CHLORO-4-AMINOQUINOLINES

A. F. Bekhli

A number of investigators [1-5] were occupied by the study of the connection between the structure and the antimalarial activity of the derivatives of 4-aminoquinoline. Chloroquine, 7-chloro-4(δ-diethylamino-α-methylbutyl)aminoquinoline, a representative of the derivatives of 4-aminoquinoline which possesses a high antimalarial activity, has been subjected to an all-inclusive study. It turned out that chloroquine does not suffer any changes after being heated to 100° in an acid medium [6], being a stable compound. Studies of the metabolism of the highly effective derivatives of 4-aminoquinoline showed that these substances are eliminated from the organism in an unchanged state, preserving the structure of their molecule [7]. Taylor and co-workers [8] found that chloroquine has antimalarial activity in vitro, i.e., under conditions which exclude an alteration of its molecule. Isomers of chloroquine which contain chlorine in positions 5, 6 or 8 showed a weak antimalarial effectiveness or its total absence in appropriate biological tests [4]. Therefore the chloro derivatives of 4-dialkylaminoalkylaminoquinoline, as well as the chloro derivatives of 9-aminoacridine [9] display a different level of antimalarial activity depending on the position of the halogen in the benzenoid part of the quinoline nucleus.

We attempted to determine whether or not the rate of hydrolytic cleavage of the amino group depends on the position of the halogen and, consequently, whether or not a connection exists between the hydrolyzability and the antimalarial activity of the derivatives of 4-aminoquinoline. An analogous problem was studied by us previously [10] with the derivatives of 9-aminoacridine and a first attempt was made to explain the different activity of the individual chlorodialkylaminoalkyl derivatives of that group by the relative stability of the link of the 9-amino group with the acridine nucleus, depending on the position of the halogen. The study of the relative rates of hydrolysis could be run, as it appeared to us, not on 4-dialkylamino derivatives of quinoline themselves but on the corresponding 4-aminoquinolines. The latter are a convenient model owing to the fact that in hydrolysis they lose ammonia, which is readily captured and may be titrated with an acid in the presence of an indicator.



For the accomplishment of the problem before us it was necessary to have 5-, 6-, 7- and 8-chloro-4-aminoquinolines; the 5-, 6- and 8-chloro derivatives were synthesized from the corresponding derivatives of 4-chloroquinoline and ammonia in phenol at 170° [11]. The isomer with the chlorine in 7-position was prepared by the method of condensation of 7-chloro-1,2,3,4-tetrahydro-4-quinolone with ammonia, developed by us earlier [12]. The 5- and 8-chloro-4-aminoquinolines were synthesized by us for the first time. 6-Chloro-4-aminoquinoline has been prepared earlier by Naito [13] by another method and turned out to be identical with our product.

In the study of the relative stability of the amino group link to the quinoline nucleus, depending on the position of the halogen in the compounds being studied, samples of equal weights were boiled with a solution of alkali. The liberated ammonia was steam distilled and determined by the usual analytical methods, by the technique which was used by us for the corresponding 9-aminoacridines [10].

The results obtained by us show that under the same conditions of hydrolysis the greatest stability is shown by 7-chloro-4-aminoquinoline, which loses the least amount of ammonia. As indicated above, its dialkylaminoalkyl derivative (chloroquine) is the most effective (Q = 15) of this important group of isomeric chloro-4-dialkylaminoalkylaminoquinolines [4]. 6-Chloro-4-aminoquinoline turns out to be less stable, losing more ammonia, than the 7-chloro isomer but less than 5- and 8-chloro isomers. Here it appeared that the effectiveness of 6-chloro-4-(δ-diethylamino-α-methylbutyl)aminoquinoline (Q = 2) is also considerably lower than the effectiveness of chloroquine and higher than the activity of the corresponding 5- and 8-chloro isomers (Q = 0.6 and 0.4).

The technique of hydrolysis used by us, as well as the possible fluctuations of the biological tests, cannot give a quantitative correlation of the biological activity of the compounds with their ability to be hydrolyzed. However on the basis of the results obtained by us one may consider that 7-chloro-4-aminoquinoline, which corresponds to the most active compound of this series and which loses the least amount of ammonia, is the most stable one under the conditions of hydrolysis. The great stability found in 7-chloro-4-aminoquinoline as well as the literature data cited above permit us to consider that chloroquine, in contrast to its poorly effective and more readily hydrolyzable isomers, displays its antimalarial action through preservation of its structure.

## EXPERIMENTAL

The chloro derivatives of 4-aminoquinoline were prepared by two methods: A) condensation of derivatives of 4-chloroquinoline with ammonia in phenol medium [11] and B) condensation of derivatives of 1,2,3,4-tetrahydro-4-quinolone with ammonia in phenol [12]. The bases prepared by us were crystallized from benzene (Table 1) and their hydrochlorides gave a basic reaction to litmus.

TABLE 1

Chloro-4-aminoquinolines and Their Hydrochlorides

| Position of the chlorine | Method of synthesis | Base | | | Hydrochloride | | |
|---|---|---|---|---|---|---|---|
| | | Yield (%) | Melting point | Found % of N** | Melting point | Found %*** | |
| | | | | | | N | Cl(ionic) |
| 5- | A | 98 | 120° | 15.54, 15.56 | 309—310° | 13.32, 13.12 | |
| 6- | A | 97 | 233—234 | 15.65, 15.62 | 302—303 | 12.96 | 16.45, 16.47 |
| 7- | B | 49 | 149.5—150* | — | 291.5—292 | 13.00 | 16.60 |
| 8- | A | 93.5 | 196—197 | 15.99, 15.91 | 287.5 | 13.01, 12.83 | 16.33, 16.37 |

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*Literature data [11]: m.p. 151°.

**$C_9H_7N_2Cl$. Calculated %: N 15.69.

***$C_9H_8N_2Cl_2$. Calculated %: N 13.02; Cl (ionic) 16.49.

Determination of relative rates of hydrolysis of chloro derivatives of 4-aminoquinoline [10]. Into a wide mouthed flask with 1 liter capacity, provided with a liquid trap and a wide straight tube in its stopper, there was placed 300 ml of distilled water and a 45% solution of sodium hydroxide (72 ml). A sample of 0.1007 g of 7-chloro-4-aminoquinoline, wrapped in foil, was introduced into the boiling alkaline solution. The wide tube was immediately stoppered. The foil dissolved rapidly in the alkali and the substance mixed with the boiling liquid. Ammonia distilled along with water into a receiver containing distilled water acidified with a measured volume of 0.01 N hydrochloric acid, and containing a few drops of methyl orange; the distillation of ammonia was immediately noted by the color change in the indicator. The ammonia distillate was titrated with hydrochloric acid as it came over. The volume of 0.01 N hydrochloric acid needed to neutralize ammonia distilled with 100, 150 and 200 ml of water was noted. The results of hydrolysis are given in Table 2.

TABLE 2

Results of Determination of Relative Rates of Hydrolysis of Isomeric Chloro-4-Aminoquinolines

| Position of chlorine | Sample (in g) | Ml of 0.01 N HCl used for neutralization of ammonia distilled with 100, 150 and 200 ml of water | | |
|---|---|---|---|---|
| | | 100 | 150 | 200 |
| 5- | 0.1003 | 5.2 | 8.4 | 14.0 |
| | 0.1021 | 5.5 | 8.3 | 12.3 |
| | 0.1001 | 5.2 | 7.8 | 12.4 |
| 6- | 0.1000 | 4.0 | 4.8 | 5.9 |
| | 0.1027 | 4.2 | 4.9 | 6.1 |
| | 0.1009 | 4.0 | 4.9 | 5.9 |
| 7- | 0.1007 | 3.3 | 3.9 | 4.8 |
| | 0.1010 | 3.2 | 4.2 | 5.2 |
| | 0.1009 | 3.0 | 3.8 | 4.9 |
| 8- | 0.1011 | 4.8 | 5.7 | 6.9 |
| | 0.1004 | 4.8 | 5.8 | 6.9 |
| | 0.1001 | 5.0 | 5.8 | 6.8 |

## SUMMARY

1. 5-, 6-, 7- and 8-chloro-4-aminoquinolines were synthesized. The relative rate of hydrolytic cleavage of ammonia in the compounds thus prepared was determined. It was found that under the conditions of hydrolysis used the greatest stability was shown by the 7-chloro isomer, which lost the smallest amount of ammonia.

2. The greatest stability of the link of the 4-amino group with the quinoline nucleus in the 7-chloro isomer, which was found in this work, in comparative reference to other isomeric compounds in this series, permits us to explain the high effectiveness of chloroquine, which is the diethylaminopentyl derivative of the indicated 7-chloro isomer, by the structural stability of its molecule under the conditions of hydrolytic decomposition.

## LITERATURE CITED

[1] O. Iu. Magidson and M. V. Rubtsov, J. Gen. Chem. 7, 1896 (1937).

[2] E. P. Gal'perin, Medical Parasitology and Parasitic Diseases, 9, 44 (1940).*

[3] H. Andersag, Ber. 81, 499 (1948).

[4] F. I. Wiselog, A Survey of Antimalarial Drugs, II, 2 (1946).

[5] E. Steck, L. Hallock and A. Holland, J. Am. Chem. Soc. 68, 1241 (1946).

[6] E. Paulini, Rev. Brasileira Malariologia, I, 49 (1953); Tropical Diseases Bulletin, 50, 1117 (1953).

[7] E. W. McChesney and others, Federation Proceedings 13, 97 (1954).

[8] D. I. Taylor and E. S. Josephson, and others, Am. J. Trop. Med. Hygiene 1, 132 (1952).

[9] K. S. Topchiev and A. F. Bekhli, Doklady Akad. Nauk SSSR 55, 635 (1947).

[10] K. S. Topchiev, A. F. Bekhli and M. L. Kirmalova, J. Gen. Chem. 19, 561 (1949).**

[11] R. Elderfield and others, J. Am. Chem. Soc. 68, 1250 (1946).

[12] A. F. Bekhli, Doklady Akad. Nauk SSSR 101, 679 (1955).

[13] T. Naito, J. Pharm. Soc. Japan. 64, 8A, 3 (1944); C. A., 45, $8528^f$ (1951).

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# AN IMPROVED METHOD OF SYNTHESIS OF DI-β,β'-CHLOROETHYL ESTER OF β-CHLOROETHYLPHOSPHONIC ACID

### E. L. Gefter

M. I. Kabachnik and P. A. Rossiiskaia [1] prepared di-β,β'-chloroethyl ester of β-chloroethylphosphonic acid by the Arbuzov isomerization of tris-β,β',β"-chloroethyl phosphite.

$$P(OCH_2CH_2Cl)_3 \xrightarrow{t^\circ} ClCH_2CH_2PO(OCH_2CH_2Cl)_2$$

However, the process of this isomerization presents a certain hazard to the experimenter since at above 150-160°, or in the presence of local spots of superheating, there begins an extremely violent reaction of an almost explosive type. The isomerization proceeds very slowly at below 150°. The yield of the isomerized product amounts to but 40% of the theoretical. The reason for this lies in the course of the reaction going simultaneously according to monomolecular (or bimolecular) and peculiar stepwise mechanisms. The latter leads to the formation of a considerable amount of undistillable sirup [2]. We succeeded in eliminating these defects from the process (the first one completely, the second in part), by running the isomerization of tris-β,β',β"-chloroethyl phosphite with energetic stirring in the presence of inert solvents (not less than 14-15% of the total weight of the mixture) with appropriate boiling points: xylene, cumene, pseudocumene, white spirits with boiling limits 150-160°. Stirring eliminates the possibility of local superheating while the solvent lowers the heat effect of the isomerization making it practically nonhazardous and at the same time it aids the monomolecular course of the reaction by separating the molecules of tris-β,β',β"-chloroethyl phosphite from each other. This leads to the increased yields of di-β,β'-chloroethyl ester of β-chloroethylphosphonic acid. In this manner we carried out the isomerization of tris-β,β',β"-chloroethyl phosphite taking into the reaction up to 2 kilograms of the substance per batch (instead of 270 g as described earlier [2]).

The safe isomerization of tris-β,β',β"-chloroethyl phosphite makes the dichloride of β-chloroethylphosphonic acid [2] a substance that is accessible in any desired amount, the same being true of derivatives of β-chloroethylphosphoric acid [3] and vinylphosphonic acid [4, 5], which was practically impossible previously. The preparation of the dichloride of β-chloroethylphosphonic acid according to Kinnear and Perren [6] is practicable for only small amounts of the substance. Below we give the results of some typical experiments with isomerization of tris-β,β',β"-chloroethyl phosphite (see table).

| $P(OCH_2CH_2Cl)_3$ (in g) | Solvent and its amount (in g) | Time of isomerization at 150-164° (in hours) | Amt. of distilled $ClCH_2CH_2PO(OCH_2CH_2Cl)_2$ in % | Undistillable residue (in g) |
|---|---|---|---|---|
| 504 | Xylene 87 | 7 | 58 | 140 |
| 40 | White spirits 40 | 17 | 50 | 17 |
| 100 | Pseudocumene 100 | 12 | 60 | 25 |
| 910 | Cumene 390 | 12 | 67 | 240 |

White spirits proved to be the least suitable of the solvents tried while cumene was the best when used in amounts of 25-30% of the total weight of the mixture.

## EXPERIMENTAL

One of typical experiments. Into a pot made of stainless steel provided with a stirrer, thermometer and a reflux condenser there was placed a mixture of 910 g of tris-β,β',β"-chloroethyl phosphite and 390 g of dry cumene. The mixture was stirred energetically and refluxed for 12 hours, during which time the boiling point of the reaction mixture gradually dropped owing to formation of ethylene chloride [2] from 158° to 153°. After cooling, cumene was distilled from the mixture (at 40-60 mm and 40-100°) and the reaction product was distilled in vacuum (4 mm) until decomposition began in the sirupy residue. The fraction with the boiling range of 155-170° (620 g) was redistilled once again and gave 610 g (67%) of pure di-β,β'-chloroethyl ester of β-chloroethylphosphonic acid. This was a colorless transparent liquid which gradually crystallized on standing; b.p. 161-163° (4 mm), $n^{20}D$ 1.4844, $d^{20}_4$ 1.3910, which values agree with the literature data [1].

Experiments with the other solvents were run analogously to the typical experiment with a small change only in the case of xylene (when a certain thermal effect was observed) the change consisting in that the mixture was rapidly heated to 130-133° and the subsequent elevation of temperature to the initial boiling of the mixture was made more slowly.

## SUMMARY

A safe method of isomerization of tris-β,β',β"-chloroethyl phosphite was developed, which permits the preparation of di-β,β'-chloroethyl ester of β-chloroethylphosphonic acid in yields of 63-67%.

## LITERATURE CITED

[1] M. I. Kabachnik and P. A. Rossiiskaia, Bull. Acad. Sci. USSR, ser. chem. 1946, 403.

[2] M. I. Kabachnik and P. A. Rossiiskaia, Bull. Acad. Sci. USSR, ser. chem., 1946, 515.

[3] M. I. Kabachnik and P. A. Rossiiskaia and N. N. Novikova, Bull. Acad. Sci. USSR, ser. chem. 1947, 97.

[4] M. I. Kabachnik, Bull. Acad. Sci. USSR, ser. chem. 1947, 233.

[5] A. H. Foord-Moore and J. H. Williams, J. Chem. Soc. 1947, 1465.

[6] A. M. Kinnear and E. A. Perren, J. Chem. Soc. 1952, 3437.

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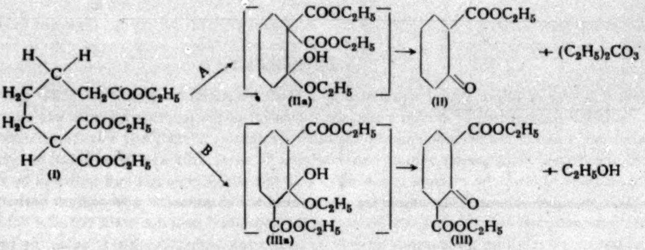
# A STUDY IN THE FIELD OF THE DIECKMANN REACTION

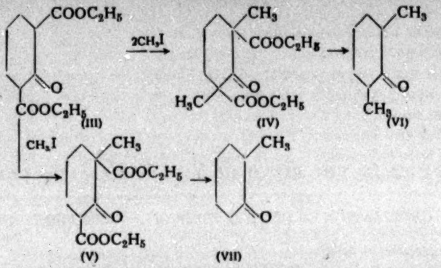
## V. CYCLIZATION OF DIETHYL ESTER OF α-CARBETHOXYPIMELIC ACID

N. S. Vul'fson and V. I. Zaretskii

During the development of some work on the investigation of the orientation of cyclization of compounds by the Dieckmann reaction [1] we studied the cyclization of diethyl ester of α-carbethoxypimelic acid. It was shown earlier [2] that in cyclization of diethyl ester of α-methylpimelic acid there is formed only 2-methyl-6-carbethoxycyclohexanone. One might expect that under the influence of the electronegative α-carbethoxy group, the cyclization of the diethyl ester of α-carbethoxypimelic acid (I) would proceed in the direction opposite to that described for the diethyl ester of α-methylpimelic acid and thus lead to the formation of 2-carbethoxycyclohexanone (II) with simultaneous cleavage of diethyl carbonate.



However in running the reaction in boiling xylene in the presence of powdered sodium we obtained 2,6-dicarbethoxycyclohexanone (III) in 57% yield. It should be noted that the cyclization of ester (I) in benzene in the presence of powdered sodium or in alcoholic solution of sodium ethoxide fails to proceed to all practical purposes (the original ester (I) is recovered) while the cyclization of tetraethyl esters of pentane- and 2-methylpentane, 1,1,5,5-tetracarboxylic acid in alcoholic solution of sodium ethoxide is accompanied by cleavage of diethyl carbonate and leads to the formation of β-keto ester (III) (yield about 35% [3]) and 3-methyl-2,6-dicarbethoxycyclohexanone (yield about 44% [1]) respectively. The formation of β-keto ester (III) in the cyclization of ester (I) is evidently explicable by the presence of steric hindrance which blocks the course of the reaction in direction A with the intermediate formation of hemiacetal (IIa), while there exists a more facile path, from the steric viewpoint, which is designated as B (above) which leads to the formation of intermediate hemiacetal (IIIa). The structure of β-keto ester (III) was proved by its methylation with methyl iodide to the corresponding 2,6-dimethyl-(IV) and 2-methyl-2,6-dicarbethoxycyclohexanone (V) with the subsequent hydrolysis and decarboxylation to the known 2,6-dimethyl-(VI) and 2-methylcyclohexanones (VII).



The initial diethyl ester of α-carbethoxypimelic acid was synthesized by us by two methods: a) starting with adipic acid, through its monoethyl ester, its silver salt and ethyl ester of δ-bromovaleric acid [4] with subsequent malonic ester synthesis, and by b) starting with 1,1,1,5-tetrachloropentane, through δ-chlorovaleric acid [5] and its ethyl ester with subsequent malonic ester synthesis according to method [6] in the presence of sodium iodide.

$$HOOC(CH_2)_4COOH \rightarrow C_2H_5OOC(CH_2)_4COOH \rightarrow C_2H_5OOC(CH_2)_4COOAg \rightarrow$$
$$\rightarrow Br(CH_2)_4COOC_2H_5$$
$$CCl_3(CH_2)_3CH_2Cl \rightarrow Cl(CH_2)_4COOH \rightarrow Cl(CH_2)_4COOC_2H_5 \rightarrow \qquad \downarrow$$
$$\rightarrow (C_2H_5OOC)_2CH(CH_2)_3CH_2COOC_2H_5$$
(I)

## EXPERIMENTAL

Monoethyl ester of adipic acid was prepared by a modified method of Swann Jr., Ehler and Buswell [7]. In order to obtain a product free of diethyl ether, the treatment of the reaction mixture was changed thus: the mixture after the reaction had been completed was left overnight at 15-20°, and was then filtered from unreacted adipic acid, the filtrate being poured into an equal volume of water, followed by addition of concentrated solution of sodium hydroxide to bring the mixture to a weakly acid test with Congo red and followed by extraction with benzene, taken in equal volume. The unreacted adipic acid was dissolved in 15% sodium carbonate solution and the solution was extracted with benzene, the extract being combined with the main benzene solution, while the adipic acid was recovered from the aqueous layer by acidification with hydrochloric acid; the recovered adipic acid was used again for the preparation of the monoethyl ester.

The benzene solution was repeatedly extracted with 15% sodium carbonate solution, then washed with water until neutral to Brilliant green paper, was then dried and distilled, collecting diethyl ester of adipic acid which was used in subsequent experiments. The sodium carbonate extract was combined with the main aqueous solution (after extraction with benzene), acidified with concentrated hydrochloric acid until strongly acidic to Congo red, extracted 4-5 times with ether, and the ethereal extract was dried with sodium sulfate and distilled in vacuum. The yield of monoethyl ester of adipic acid was 61.8% (taking into account the recovery of adipic acid); b.p. 129-132.5° at 2 mm; m.p. (freezing) 27.4°. According to literature data, b.p. 155-157° at 7 mm [7], m.p. 29.9°[4].

Ethyl ester of δ-bromovaleric acid. This was prepared from monoethyl ester of adipic acid according to [4]: a) silver salt, yield 70% (calculated on silver salt of monoethyl adipate), b.p. 71° at 2 mm, 69.5° at 1.5 mm, $n^{20}D$ 1.4605, $d^{20}_4$ 1.3085. According to literature data: b.p. 101-103° at 10 mm [4], $n^{20}D$ 1.4582, $d^{20}_4$ 1.3043 [8].

δ-Chlorovaleric acid. This was prepared by hydrolysis of 1,1,1,5-tetrachloropentane [5]. The starting material had b.p. 64.5-70.25° at 2.5 mm, $n^{20}D$ 1.4865, $d^{20}_4$ 1.3430. According to the literature data: b.p. 112° at 24 mm, $n^{25}D$ 1.4859, $d^{25}_4$ 1.3416 [9]. The yield of δ-chlorovaleric acid was 52.5%; b.p. 101.5° at 2.5 mm, 101.5° at 2 mm, freezing point 18.25°, $n^{20}D$ 1.4545, $d^{20}_4$ 1.1644. According to literature data: b.p. 122-124° at 8 mm, $n^{25}D$ 1.4525, $d^{25}_4$ 1.1667 [5]; m.p. 18° [10].

Ethyl ester of δ-chlorovaleric acid. A mixture of 95 g of δ-chlorovaleric acid, 300 ml of benzene, 70 ml of anhydrous alcohol and 13.5 ml of concentrated sulfuric acid was refluxed for six hours, cooled, poured into 500 ml of water, the mixture being then neutralized with 15% sodium carbonate solution until alkaline to Brilliant yellow paper, the benzene layer washed with water until neutral to Brilliant yellow paper, then dried with sodium sulfate and distilled, yielding 99 g (86%) of the ester with b.p. 53.5° at 1.5 mm, 52.5° at 1 mm, $n^{20}D$ 1.4305, $d^{20}_4$ 1.0518. According to the literature data: b.p. 90° at 13 mm, $d^{20}$ 1.054 [10].

Ethyl ester of α-carbethoxypimelic acid. a) From ethyl ester of δ-bromovaleric acid. Malonic ester (117 g) was added to the solution of sodium ethoxide (from 5.4 g of sodium and 100 ml of anhydrous alcohol) and the solution was heated to boiling (about 85°) while over thirty minutes 49.2 g of ethyl ester of δ-bromovaleric acid was being added dropwise. The mixture was refluxed three hours longer (pH of the solution was about 7.5), the alcohol was distilled from it (finally under slight vacuum), the residue was cooled, poured into 200 ml of water, extracted with benzene (200 and 100 ml portions used), the benzene solution was washed with water, dried over sodium sulfate and distilled. The yield of the ethyl ester of α-carbethoxypimelic acid was 75.5%; b.p. 146.5-150° at 2 mm, $n^{20}D$ 1.4380, $d^{20}_4$ 1.0561. According to the literature data: b.p. 147-149° at 2 mm, $n^{20}D$ 1.4389, $d^{20}_4$ 1.0568 [6].

b) From ethyl ester of δ-chlorovaleric acid. The product was prepared by method [6]; yield 83%, b.p. 142-143° at 1 mm.

Cyclization of diethyl ester of α-carbethoxypimelic acid. To the suspension of 4.7 g of powdered sodium in 150 ml of dry xylene there was added rapidly 43.2 g of ethyl ester of α-carbethoxypimelic acid and 0.3 ml of anhydrous alcohol. The mixture was stirred energetically until the termination of self-heating of the mass (about 10 minutes; the temperature rises to 68°), after which it was heated on an oil bath at the boiling point (134.5°) and refluxed with stirring until the boiling point of the reaction mixture ceased to decline (5-6 hours; the boiling point drops to about 112°). The mixture was cooled, poured into 150 g of ice, cooling externally with ice-salt mixture (the temperature of the reaction mass should be from −5° to −7°) and neutralized with dilute hydrochloric acid (1 : 1) to acid test with Congo red (at temperature of −1.5° to −3°). The layers were separated, the aqueous layer was extracted with 75 ml of benzene, the combined organic layer was washed with 30 ml of 5% sodium carbonate, then with water until neutral to Brilliant yellow paper, dried over sodium sulfate, freed of the solvent by distillation, and the residue was distilled, collecting the following fractions: 1st b.p. 92° at 3 mm, 136.5° at 3.5 mm, 2.4 g, $n^{20}D$ 1.4730; 2nd b.p. 136.5-138° at 3.5 mm, 2.9 g, $n^{20}D$ 1.4760; 3rd b.p. 138-140° at 3.5 mm, 15.9 g, $n^{20}D$ 1.4750, $d^{20}_4$ 1.1203, $MR_D$ 60.87 (calculated for the enol 59.78; calculated for the ketone 58.74); 4th b.p. 144-150° at about 5 mm, 0.6 g, $n^{20}D$ 1.4735; 5th b.p. 150° at 4.5 mm, 152° at 6-7 mm (with decomposition), 1.7 g, $n^{20}D$ 1.4740.

Analysis of the 3rd fraction:

Found %: C 59.66; H 7.56. $C_{12}H_{18}O_5$. Calculated %: C 59.50; H 7.44.

The first, fourth and fifth fractions were combined and redistilled obtaining thereby an additional 1.9 g of the keto ester (III) with b.p. 139-142° at 3.5 mm, $n^{20}D$ 1.4755 (6th fraction). All the fractions collected were colorless and gave an intensely violet color with ferric chloride. The second, third and sixth fractions thickened after some time owing to the separation of crystals of the keto form [3]. The yield of 2,6-dicarbethoxycyclohexanone (fractions 2, 3 and 6) was 57%. According to the literature data: b.p. 165-175° at 12 mm, 165-165.5° at 12 mm (enol), $n^{18.5}D$ 1.4692, $d^{18.5}_4$ 1.1239 [3].

1-Phenyl-3,4,1',2'-hexahydrobenzo-3-carbethoxy-5-pyrazolone. A mixture of 1.2 g of 2,6-dicarbethoxycyclohexanone and 0.55 g of phenylhydrazine was heated on a steam bath for one hour. It was then cooled to 15-20° and dissolved with stirring in 2 ml of ether. Approximately an hour after there began the crystallization of the pyrazolone. The mixture was left overnight, filtered and washed with ether. The yield was 1.23 g (86%); m.p. 150-150.5°; after boiling in ether, m.p. 151-151.5°. According to the literature data: m.p. 151-152° [3].

2,6-Dimethyl-2,6-dicarbethoxycyclohexanone. To the cooled solution of 17 g of 2,6-dicarbethoxycyclohexanone in 34 ml of anhydrous methanol there was added 12 ml of methyl iodide, the mixture being cooled to −15°, after which a solution of sodium methoxide (from 3.5 g of sodium and 42 ml of anhydrous methanol) was added over about 5 minutes with stirring at the temperature of from −15° to −7°. The mixture was stirred for four hours at the temperature of −2° to 0° and was left overnight at about 0°. It was then refluxed, again with stirring, until it became neutral to Brilliant yellow test paper (2 hours), after which the methanol was distilled from the mixture on a steam bath (the volume of distillate was about 65 ml). The residue was cooled, poured into 300 ml of water, extracted four times with ether and the ethereal extract washed with 15% potassium hydroxide solution (three times with 25 ml) and with water until neutral. The solution was dried over sodium sulfate, the ether was distilled from it and the residue was distilled yielding 2,6-dimethyl-2,6-dicarbethoxycyclohexanone in 14.1 g yield (75%); b.p. 113-116° at 2 mm, $n^{20}D$ 1.4620-1.4625; the product contains traces of the unmethylated material since it gives a barely visible color test with ferric chloride, which appears after 3-5 minutes. For purification the product was dissolved in 300 ml of ether and was washed with cold 15% potassium hydroxide solution until the test with ferric chloride became negative (15 washes with 25 ml each), followed by washing with water until neutral to Brilliant yellow test paper, after which it was dried and distilled yielding 9.8 g of pure 2,6-dimethyl-2,6-dicarbethoxycyclohexanone; b.p. 123.5-126.5° at 3 mm, $n^{20}D$ 1.4615, $d^{20}_4$ 1.086, $MR_D$ 67.84 (the calculated value is 67.97). According to the literature data: b.p. 142° at 6 mm [11].

2,6-Dimethylcyclohexanone. A hot solution of 11 g of potassium hydroxide (8.7 g calculated as 100% substance) in 16.5 ml of anhydrous methanol was chilled rapidly to −5° and to the resulting thin suspension there was added with stirring and cooling to from −5° to +1° a solution of 8.8 g of 2,6-dimethyl-2,6-dicarbethoxycyclohexanone in 12 ml of anhydrous methanol. The mixture was stirred at 18-20° for about three hours and was left at this temperature for 12 days. The reaction mixture was then poured into 150 ml of water (at about 10°) and extracted with ether three times; the ethereal extract was washed with water until neutral to Brilliant yellow test paper. The aqueous layer combined with the wash waters from the ethereal layers was treated with 60 ml of concentrated sulfuric acid and was steam distilled. The distillate was extracted five times with ether, the ethereal solution was added to the extract from the alkaline reaction mixture (after pouring into water) and the combined ethereal solution was dried over sodium sulfate and distilled, yielding 2,6-dimethylcyclohexanone; yield 2.1 g (50.5%; b.p. 167-170.5° at 743 mm, $n^{20}D$ 1.4475-1.4480, $d^{20}_4$ 0.9087. According to the literature data: b.p. 170-172°, $n^{20}D$ 1.4481, $d^{20}_4$ 0.9122 [12]. Semicarbazone, m.p. 181-182° (from anhydrous alcohol). According to literature data: m.p. 183° [13].

Found %: C 59.12; H 9.52. $C_9H_{17}ON_3$. Calculated %: C 59.03; H 9.29.

2-Methyl-2,6-dicarbethoxycyclohexanone. To a cooled solution of 18.2 g of 2,6-dicarbethoxycyclohexanone in 34 ml of anhydrous methanol there was added 6.5 ml of methyl iodide, the mixture was cooled to −16° and treated with stirring at from −16° to −12.5° over seven minutes with a solution of sodium methoxide (from 1.9 g of sodium in 30 ml of anhydrous methanol) after which the mixture was left overnight at −3°. Then the mixture was refluxed for one hour, freed of methanol by distillation, the residue was cooled, poured into 300 ml of water, extracted four times with ether, the ethereal solution was washed with water and dried with anhydrous sodium sulfate. Ether was distilled from this solution and the residue was distilled in vacuum yielding 2-methyl-2,6-dicarbethoxycyclohexanone; yield 14 g (72.8%), b.p. 112-114° at 1 mm (by the literature data b.p. 142-145° at 6 mm [11]), $n^{20}D$ 1.4645-1.4655, $d^{20}_4$ 1.0986; the substance gave an intense violet color with ferric chloride; $MR_D$ 64.21 (for the enol of calculated value is 64.40; for the ketone it is 63.37).

2-Methylcyclohexanone. 2-Methyl-2,6-dicarbethoxycyclohexanone (14 g) was hydrolyzed and decarboxylated analogously to 2,6-dimethyl-2,6-dicarbethoxycyclohexanone and yielded 2-methylcyclohexanone in a 2.3 g yield (37.3%); b.p. 162.5-166° at 730 mm, $n^{20}D$ 1.4485, $d^{20}_4$ 0.9224. According to the literature data: b.p. 166°, $n^{20}D$ 1.4483, $d^{20}_4$ 0.9231 [15]. Semicarbazone, m.p. 188.5-189° (from anhydrous alcohol). According to the literature data: m.p. 189° [16]. It did not give a depression in a mixed melting point with the semicarbazone of 2-methylcyclohexanone.

## SUMMARY

The cyclization of diethyl ester of $\alpha$-carbethoxypimelic acid in the Dieckmann reaction was investigated. It was shown that the primary reaction product is 2,6-dicarbethoxycyclohexanone. The structure of 2,6-dicarbethoxycyclohexanone was proved by its methylation with methyl iodide to the mono- and the dimethyl derivatives and by the subsequent hydrolysis and decarboxylation of these to 2-methyl- and 2,6-dimethylcyclohexanones, respectively.

## LITERATURE CITED

[1] V. I. Zaretskii and N. S. Vul'fson, J. Gen. Chem. 28, 388 (1958).*

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* Original Russian pagination. See C. B. Translation.

[2] N. S. Vul'fson and V. I. Zaretskii, J. Gen. Chem. 28, 369 (1958).*

[3] M. I. Ushakov, J. Russ. Phys. Chem. Soc. 61, 797 (1929).

[4] J. O. Jilek and V. Michajlyszyn, Chem. Listy, 48, 1210 (1954); C. A. 1954, 9507$^{-h}$.

[5] R. M. Joyce, W. E. Hanford and J. Harmon, J. Am. Chem. Soc. 70, 2531, 2529 (1948).

[6] A. N. Nesmeianov and L. N. Zakharkin, Bull. Acad. Sci. USSR, ser. chem. 1955, 228.*

[7] Syntheses of organic preparations, vol. 2, 345, 346 (1949). **

[8] N. J. Leonard and W. E. Goode, J. Am. Chem. Soc. 72, 5404 (1950).

[9] R. M. Joyce, W. E. Hanford and J. Harmon, J. Am. Chem. Soc. 70, 2529 (1948).

[10] H. Norman and G. Voreux, Comptes rend 231, 703 (1950).

[11] S. M. Mukherjee, J. Indian Chem. Soc. 24, 495 (1947).

[12] L. Ruzicka and D. R. Koolhaas, A. H. Wind, Helv. Chim. Acta. 14, 1164 (1931).

[13] R. Cornubert and P. Anziani, Comptes rend 217, 197 (1943).

[14] A. Skita, Ber. 56, 1016 (1923).

[15] A. J. Vogel, J. Chem. Soc. 1938, 1323.

[16] R. Kuhn and H. J. Haas, Lieb. Ann. 600, 152 (1956).

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*Original Russian pagination. See C. B. Translation.

**In Russian.

# REPLACEMENT OF HALOGEN IN AZO COMPOUNDS

## I. REPLACEMENT OF CHLORINE IN 2-CHLOROPHENYLAZO-2'-NAPHTHOL BY ALKOXY GROUPS

B. I. Stepanov, M. A. Salivon, V. F. Lagidze and L. A. Dediukhina

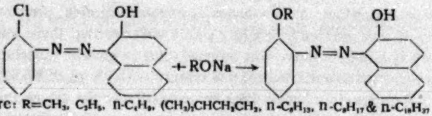
As is known [1], the replacement of an aromatically bound atom of halogen by other substituents is realized with considerably more difficulty than the analogous reactions in the aliphatic series and it is only the activating influence on the part of electrophilic substituents as well as the catalytic action of copper and its compounds that make it possible for one to conduct the substitution reactions at temperatures under 200°.

The data on the effect of the azo group on the mobility of an aromatically bound halogen are scanty. According to Borsche and Exss [2], an azo group in the molecules of isomeric mononitrochlorobenzenes facilitates the replacement of chlorine in the reaction with amines and alcoholates, but it does so to a lesser degree than do the nitro, nitrile and the carboxyl groups. According to Badger, Cook and Vidal [3], the introduction of an azo group into the molecule of chlorobenzene increases the yield of the substitution product of chlorine in the reaction with piperidine by approximately 1.5-fold while the nitro group under these conditions increases the yield by almost 10-fold. According to the patent data of Sieglitz and co-workers [4, 5], the replacement of chlorine and bromine in the molecules of azo dyes, which do not contain any electrophilic substituents in ortho- and para-positions in respect to these atoms, by alkoxy groups and residues of alkyl- and arylsulfinic acids requires the temperature of the order of 130-170° and, in a number of cases, the presence of copper powder. At the same temperature the replacement of chlorine by the hydroxy group proceeds in the molecule of an azo dye containing a carboxy group in ortho-position in respect to the atom of chlorine [6] and only the presence of nitro and sulfo groups in ortho- and para-positions with respect to the chlorine atom permits one to realize such a substitution at the boiling point of an alkaline aqueous solution of the azo dye [7].

For these reasons there is much interest in the patents by D. Delfs and co-workers [8-10] according to which the chlorine atom in molecules of o-chloro-o'-hydroxy- azo dyes is replaced in the presence of copper salts by hydroxy, alkoxy, alkylamino and some other groups by even brief heating with aqueous alkalies, alcoholates etc. at temperatures of the order of 70-100°. The amount of copper salt used in the process exceeds by a large margin that used for catalytic reactions, while, according to the patent data, the end product is obtained in the form of a copper complex. Only the chlorine atom in ortho-position in respect to the azo group suffers the replacement (as, for example, it is in examples of Sieglitz patents [4, 5]). The significance of copper is underlined by the circumstance that the replacement of chlorine by a hydroxy group in the same dyes in aqueous alkaline solution but in the presence of chromium oxide [11] (with formation of chromium-bearing complexes) requires the temperature of the order of 130-140°. The data of the patent by Schmelzer and Bayer [12] are in the state of known contradiction with those of Delfs' patent, as the former indicate that the formation of copper complexes of o,o'-dihydroxy azo dyes, in the reaction of o-chloro-o'-hydroxy azo dyes with alkalies and copper salts, proceeds only at temperatures of 140-150°.

Considering the theoretical significance of the problem of the reasons for the anomalous mobility of the halogen atoms located in the ortho-position in respect to the azo group, as well as the preparative possibilities opened by this reaction, since the resulting azo dyes are subject to facile reduction cleavage, we considered it interesting to study the reaction in more detail, especially since the data on the replacement of the halogen in azo compounds are contained almost totally in the patent literature.

We used 2-chlorophenylazo-2'-naphthol, i.e., the azo dye from 2-chloroaniline and 2-naphthol, for the starting o-halo-o'-hydroxy azo compound. In its reaction with sodium methoxide, prepared either by the action of metallic sodium or sodium hydroxide on methyl alcohol, and copper sulfate in methyl alcohol there was prepared in quantitative yield the 2-methoxyphenylazo-2'-naphthol in the form of the complex compound with copper, after heating under a reflux condenser on a water bath. The free methoxy substituted dye was readily liberated by the decomposition of the complex by heating with hydrochloric acid. In a control experiment, in the absence of copper sulfate, there was isolated only the starting chlorine-containing dye. Analogous results were obtained in the reaction of the original dye with sodium ethoxide in ethyl alcohol. Here, also in the presence of copper sulfate, the chlorine atom was quantitatively replaced by the ethoxy group at the boiling point of the reaction mixture (heating on a water bath). The reaction of the chlorine-containing dye with alcoholates of higher boiling alcohols – n-butyl, isoamyl, n-hexyl and n-octyl – was run in an excess of the appropriate alcohol at 100-110°, while the reaction with the alcoholate of octadecyl alcohol was run in toluene medium at 115-118°. Products of replacement of chlorine by the alkoxy groups were obtained in high yields in all cases, while the control experiments, in the absence of the copper salt, gave negative results.



where: R=$CH_3$, $C_2H_5$, n-$C_4H_9$, $(CH_3)_2CHCH_2CH_2$, n-$C_6H_{13}$, n-$C_8H_{17}$ & n-$C_{18}H_{37}$

In this manner the reaction is realized in the presence of a copper salt quite readily, which fact speaks for the high order of mobility of the chlorine atom in the given dye under the above conditions.

Some of the dyes prepared by us turned out to be suitable for dyeing acetate and polyamide fibers by the suspension technique.

The corresponding ethers of o-aminophenol (2-alkoxyanilines), which were characterized in the form of hydrochloride salts of benzoyl derivatives, except for the ether with the octadecyl residue which was quite stable in the form of the free base, owing to the facile oxidizability of the majority of these ethers, were prepared by the reductive cleavage of the alkoxy substituted dyes. It is interesting to note that the free base of this amine (2-octadecoxyaniline) is formed already in the process of recrystallization of its hydrochloride salt from methy alcohol. Among the ethers of o-aminophenol prepared by us, the ethers with butyl [13, 14], isoamyl [15], n-hexyl [14] and n-octyl [14] residues, have been described previously in the form of free bases.

## EXPERIMENTAL*

The starting dye was prepared by diazotization of 2-chloroaniline and coupling with 2-naphthol; m.p. 167° (from glacial acetic acid [16]).

Replacement of chlorine by methoxy group. Four g of the starting dye, ground with 2 g of copper sulfate, was introduced into the solution of sodium methoxide prepared by the reaction of 1 g of metallic sodium (or 2.5 g of sodium hydroxide) with 40 ml of methyl alcohol. The mixture was refluxed for four hours with stirring on a water bath, after which the alcohol was distilled off and the residue was boiled for 15-20 minutes with 50 ml of concentrated hydrochloric acid. After dilution with water, the precipitate was filtered off, washed until the filtrate became free of chloride ions and dried at 70°. Its weight was 3.9 g (100%). After recrystallization from glacial acetic acid the dye was obtained in the form of orange-red bronze-appearing powder with m.p. 178°. The test for chlorine was negative. A mixed melting point with the azo dye from o-anisidine and 2-naphthol (m.p. 178°; the literature indicates m.p. 180° – from glacial acetic acid [16], or 178° – from alcohol [17]) showed no depression.

Replacement of chlorine by ethoxy group. The amounts of the starting materials, selected appropriately, and the conditions for running the reaction and working-up the product were the same as in the above experiment; the duration of heating on the water bath was six hours. There was obtained 3.9 g (94.4%) of copper-free dye.

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*With participation by V. S. Zenkevich.

After recrystallization from glacial acetic acid the dye was obtained in the form of a red shiny powder with m.p. 145°. The test for chlorine was negative. A mixed melting point with the azo dye from o-phenetidine and 2-naphthol, which melted at 145° (the literature indicates m.p. 145° – from glacial acetic acid [16] and 138° – from alcohol [17]) showed no depression.

Replacement of chlorine by n-butoxy group. Eight g of the starting dye, ground with 4 g of copper sulfate, was introduced into the solution of sodium butoxide prepared by the action of 2 g of metallic sodium on 80 ml of n-butyl alcohol (b.p. 117°) and the mixture was heated with stirring for eight hours at 100°. After that the reaction mixture was diluted with 200 ml of water and brought to boiling. After cooling, the precipitate was filtered off and boiled for 20 minutes with 100 ml of concentrated hydrochloric acid. The precipitate was filtered off after dilution with water, washed until the filtrate became free of the chloride ions and dried at 70°. Its weight was 8.5 g (93.8%). After recrystallization from glacial acetic acid the dye was obtained in the form of red needle shaped crystals, m.p. 116-117°. The test for chlorine was negative. The dye was soluble in benzene, toluene, glacial acetic acid, methyl and ethyl alcohols and insoluble in water.

Found %: C 75.48, 75.28; H 6.51, 6.41; N 9.04; 8.86. $C_{20}H_{20}O_2N_2$. Calculated %: C 75.00; H 6.25; N 8.75.

Preparation of 2-butoxyaniline. To a solution of stannous chloride, prepared by the reaction of 8 g of metallic tin with 75 ml of concentrated hydrochloric acid with heating, there was added 70 ml of water and 5 g of the butoxy substituted dye. The mixture was refluxed until it became colorless, after which it was left overnight. The resulting precipitate was filtered off and treated with 25 ml of 5% solution of sodium hydroxide to which had been added about 0.3 g of sodium hydrosulfite for protection of the amine from oxidation. 2-Butoxyaniline was extracted with ether and, after separation of the ethereal layer, was precipitated by a stream of hydrogen chloride passed into the solution. The precipitate was filtered off and recrystallized from ethyl alcohol. There was obtained 1.9 g of the hydrochloride salt in the form of long thin plates, m.p. 146-148°.

Found %: N 7.15, 7.09. $C_{10}H_{16}ONCl$. Calculated %: N 6.94.

For preparation of the N-benzoyl derivative, 0.15 g of the hydrochloride salt of 2-butoxyaniline was shaken for ten minutes with 2 ml of 20% solution of sodium hydroxide and 0.5 ml of benzoyl chloride, after which the mixture was diluted with water and the precipitate was filtered off, washed and dried. Its weight was 0.15 g. After recrystallization from dilute methyl alcohol, the benzoyl derivative was obtained in the form of greatly attenuated flat hexagons; m.p. 45-46°.

Found %: C 75.68, 75.80; H 7.36, 7.22; N 5.39, 5.31. $C_{17}H_{19}O_2N$. Calculated %: C 75.83; H 7.06; N 5.20.

Replacement of chlorine by 3-methylbutoxy group. The amounts of the starting materials (isoamyl alcohol with b.p. 132°) and the conditions of running the reaction were as in the previous experiment. The reaction mixture was diluted with water, the precipitate was filtered off, boiled twice with water, then for fifteen minutes with 100 ml of concentrated hydrochloric acid. After dilution with water the reaction product was precipitated in the form of a tarry viscous mass which hardened on cooling. The precipitate was ground up and again treated with concentrated hydrochloric acid (50 ml) for fifteen minutes at reflux with stirring. The again triturated precipitate was washed with water until the filtrate became clear of chloride ions and was dried in air. Its weight was 6.5 g (68.8%). After recrystallization from glacial acetic acid and acetone the dye was obtained in the form of bundles of thin needles; m.p. 128°. The test for chlorine was negative. The dye is soluble in benzene, toluene, methyl and ethyl alcohols, glacial acetic acid; it is insoluble in water.

Found %: C 75.2, 75.31; H 7.07, 6.96; N 8.64, 8.51. $C_{21}H_{22}O_2N_2$. Calculated %: C 75.45; H 6.58; N 8.38.

Preparation of 2(3'-methylbutoxy)aniline. To a solution of stannous chloride (from 2 g of metallic tin and 20 ml of concentrated hydrochloric acid) there was added 20 ml of water and 1 g of the methylbutoxy substituted dye and the mixture was refluxed until it became colorless. The reaction mixture was made alkaline with 30 ml of 40% solution of sodium hydroxide (with addition of 0.3 g of sodium hydrosulfite) and methylbutoxyaniline was steam distilled and extracted from the distillate with ether. The ethereal layer was separated and treated with 5 ml of concentrated hydrochloric acid. After evaporation of ether and concentration of the residue on a steam bath there was obtained 0.45 g of the hydrochloride salt of (2(3'-methylbutoxy)-aniline in the form of thin colorless needles (after recrystallization from water acidified by a few drops of hydrochloric acid); m.p. 165-165.5°.

Found %: N 6.69. $C_{11}H_{18}ONCl$. Calculated %: N 6.49.

For preparation of the n-benzoyl derivative 0.1 g of the hydrochloride of 2(3'-methylbutoxy)aniline was benzoylated as in the case of 2-butoxyaniline. There was obtained 0.16 g of the benzoyl derivative; flat colorless needles, after recrystallization from methyl alcohol; m.p. 58-59°.

Found %: C 76.51, 76.37; H 7.51, 7.65; N 4.96; 5.08. $C_{18}H_{21}O_2N$. Calculated %: C 76.32; H 7.42; N 4.95.

*Replacement of chlorine by hexoxy group.* The amounts of the starting dye, copper sulfate and metallic sodium and the conditions for running the reaction were the same as in experiments with butyl and isoamyl alcohols; n-hexyl alcohol, b.p. 157°, was taken in the volume of 40 ml. After cooling of the reaction mixture the precipitate was filtered off, the hexyl alcohol was distilled in vacuum from the filtrate and the residue was combined with the main precipitate. The product was boiled twice with water, then with concentrated hydrochloric acid (100 ml), after which the mixture was diluted with water, the dye was filtered off, washed until the filtrate became free of chloride ions, and dried in air. Its weight was 8.75 g (88.8%). After recrystallization from glacial acetic acid and acetone the dye was obtained in the form of flat elongated rectangles; m.p. 90-90.5°. The test for chlorine was negative. The dye is soluble in toluene, methyl and ethyl alcohols, acetone and glacial acetic acid; it is insoluble in water.

Found %: C 75.51, 75.41; H 6.62, 6.79; N 8.12, 8.08. $C_{22}H_{24}O_2N_2$. Calculated %: C 75.86; H 6.90; N 8.05.

*Preparation of 2-hexoxyaniline.* The reductive cleavage of the hexoxy substituted dye and the isolation of the hydrochloride salt of 2-hexoxyaniline were run as in the preparation of 2(3'-methylbutoxy)aniline. After recrystallization from dilute methyl alcohol the hydrochloride salt of 2-hexoxyaniline was obtained in the form of colorless needles, m.p. 159-159.5°.

Found %: N 6.25. $C_{12}H_{20}ONCl$. Calculated %: N 6.10.

For preparation of the N-benzoyl derivative 0.1 g of the hydrochloride salt of 2-hexoxyaniline was benzoylated as in the case of 2-butoxyaniline. There was obtained 0.13 g of the benzoyl derivative; flat colorless needles, after recrystallization from methyl alcohol; m.p. 48-48.5°.

Found %: C 76.97, 76.85; H 7.95, 7.87; N 4.89, 4.81. $C_{19}H_{23}O_2N$. Calculated %: C 76.76; H 7.74; N 4.71.

*Replacement of chlorine by octoxy group.* The amounts of the starting materials were the same as in the experiment with hexyl alcohol, except for the use of n-octyl alcohol (b.p. 194-195°) and heating for ten hours at 110-115°. After termination of heating, the reaction mixture was diluted with water with energetic stirring, and the precipitate was filtered off. The filtrate rapidly separated into layers and the alcohol layer was separated and freed of octyl alcohol in vacuum at 105-110°. The residue was combined with the main precipitate. The combined product was boiled for 30 minutes with 100 ml of concentrated hydrochloric acid, after which the mixture was cooled, diluted with water, the dye was filtered off and freed of chloride ions by washing and repeated boiling with water. Its weight was 9.5 g (89.2%). After recrystallization from ethyl alcohol the dye was obtained in the form of bundles of thin needles; m.p. 98.5°. The test for chlorine was negative. The dye is readily soluble in the cold in carbon tetrachloride, chloroform, benzene and toluene; in hot acetone, ethyl and methyl alcohols; it is insoluble in water.

Found %: C 76.41, 76.50; H 7.76, 7.65; N 7.63. $C_{24}H_{28}O_2N_2$. Calculated %: C 76.59; H 7.45; N 7.45.

*Preparation of 2-octoxyaniline.* The reductive cleavage of the octoxy substituted dye was run as in the preparation of 2(3'-methylbutoxy)aniline. The reaction mixture, along with the dark oily liquid which separated from it and solidified on cooling, was diluted with 70 ml of water and treated with 30 ml of 40% solution of sodium hydroxide (with addition of 0.3 g of sodium hydrosulfite), after which the 2-octoxyaniline was extracted with ether. After addition of 5 ml of concentrated hydrochloric acid and 20 ml of water to the ethereal layer there precipitated a slightly pinkish precipitate of the hydrochloride salt, which was filtered off and dried in air. After recrystallization from methyl alcohol the hydrochloride salt of 2-octoxyaniline was obtained in the form of colorless needles; m.p. 142-142.5°.

Found %: C 65.27, 65.38; H 9.24, 9.16; N 5.54, 5.63. $C_{14}H_{24}ONCl$. Calculated %: C 65.63; H 9.32; N 5.43.

For preparation of the N-benzoyl derivative 0.1 g of the hydrochloride salt of 2-octoxyaniline was benzoylated as in the case of 2-butoxyaniline. There was obtained 0.14 g of the benzoyl derivative which formed colorless platelets after recrystallization from dilute methyl alcohol; m.p. 43.5-44°.

Found %: C 77.37, 77.43; H 8.52, 8.46; N 4.47, 4.59. $C_{21}H_{27}O_2N$. Calculated %: C 77.53; H 8.30; N 4.30.

Replacement of chlorine by octadecoxy group. Four g of the initial dye was triturated with 2 g of copper sulfate and thoroughly mixed with 40 ml of toluene. The resulting suspension was introduced into a solution of sodium octadecoxide (prepared by the reaction of 20 g of n-octadecyl alcohol (m.p. 58.5°) with 1.5 g of metallic sodium at 150-160°) preheated to 95°. The mixture was heated for eleven hours at 95-100° and nine more hours at 115-118°, during which a foaming of the reaction mixture was observed. After that the toluene was distilled in vacuum, the residue was diluted with water and the precipitate was filtered off. For removal of the excess octadecyl alcohol the precipitate was treated several times with boiling methyl alcohol (total volume 300 ml), after which it was boiled for 30 minutes with 100 ml of hydrochloric acid. After dilution with water the precipitate was filtered off, washed with hot water until free of chloride ions, boiled several times with methyl alcohol (total volume 250 ml) and dried. Its weight was 5.2 g (71.2%). After recrystallization from glacial acetic acid the dye was obtained in the form of bundles of thin needles; m.p. 78.5-79.5°. The test for chlorine was negative. The dye is soluble in cold benzene, toluene, carbon tetrachloride and chloroform; in hot acetone and acetic acid; it is insoluble in water, methyl and ethyl alcohols.

Found %: C 79.18, 79.29; H 9.48, 9.36; N 5.45. $C_{34}H_{48}O_2N_2$. Calculated %: C 79.07; H 9.30; N 5.42.

Preparation of 2-octadecoxyaniline. The reductive cleavage of the octadecoxy substituted dye was run as described for the 2(3'-methylbutoxy)aniline. The precipitate formed as the result of solidification of the dark oily liquid collected on the bottom of the flask after reduction was separated, washed with water and treated with 25 ml of 5% solution of sodium hydroxide (with addition of 0.3 g of sodium hydrosulfite). Then 2-octadecoxyaniline was extracted with ether and the ethereal solution was treated with 5 ml of concentrated hydrochloric acid. After evaporation of ether, the precipitate of the hydrochloride salt of 2-octadecoxyaniline was filtered off, washed with water and dried in air. M.p. 124-125.5°.

Found %: N 3.54. $C_{24}H_{44}ONCl$. Calculated %: N 3.52.

After recrystallization of the hydrochloride salt from methyl alcohol there was isolated a quantitative yield of the free 2-octadecoxyaniline in the form of flat plates; m.p. 54.5-55.5°.

Found %: C 79.59, 79.66; H 12.09; 12.01; N 3.67, 3.65. $C_{24}H_{43}ON$. Calculated %: C 79.77; H 11.91; N 3.87.

For preparation of the N-benzoyl derivative 0.1 g of the hydrochloride salt of 2-octadecoxyaniline was benzoylated as in the case of 2-butoxyaniline. There was obtained 0.12 g of the benzoyl derivative; flat needles after recrystallization from methyl alcohol; m.p. 66.7-68°.

Found %: C 79.81; 79.93; H 10.23, 10.28; N 2.92. $C_{31}H_{47}O_2N$. Calculated %: C 80.00; H 10.10; N 3.01.

We express our gratitude to N. N. Vorozhtsov for a number of valuable suggestions.

## SUMMARY

1. The replacement of chlorine atoms by alkoxy groups with methyl, ethyl, n-butyl, isoamyl, n-hexyl, n-octyl and n-octadecyl residues was realized by the reaction of sodium alcoholates with the azo dye from 2-chloroaniline and 2-naphthol.

2. It was shown that the reaction of chlorine replacement in the given o-halo-o'-hydroxy azo dye proceeds under mild conditions in the presence of a copper salt.

3. 2-Alkoxyanilines with n-butyl, isoamyl, n-hexyl, n-octyl and n-octadecyl residues were prepared by reductive cleavage of the alkoxy substituted dyes.

## LITERATURE CITED

[1] N. N. Vorozhtsov, Bases of synthesis of intermediates and dyes, State Chemical Press, pp. 334 (1955).*

[2] W. Borsche and F. Exss, Ber. 56, 2353 (1923).

[3] G. M. Badger, J. W. Cook and W. P. Vidal, J. Chem. Soc. 1947, 1109.

[4] German Patent 605,974; Friedlander 21, 962.

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*In Russian.

[5] German Patent 623,650; Friedlander 22, 879.

[6] German Patent 278,613; Friedlander 12, 323.

[7] German Patent 141,538; Friedlander 6, 1323.

[8] German Patent 571,859; Friedlander 19, 1689.

[9] German Patent 738,900; Ch. A. 39, 5502 (1945).

[10] German Patent 658,841; Friedlander 24, 679.

[11] German Patent 576,546; Friedlander 20, 1172.

[12] Federated German Republic Patent 843,124; Chem. Abstr. 49, 3544 (1955).

[13] E. Profft, Chem. Ztg. 2, 194 (1950); Ch. A. 45, 7544 (1951).

[14] R. Nodzu, H. Watanabe, S. Oka, C. Nagaischi, T. Teramatsu, H. Arima, M. Kōgame and K. Kobayashi, J. Pharm. Soc. Japan, 71, 713 (1951); Ch. A. 46, 3976 (1952).

[15] S. S. Marathe, N. S. Limaye and B. V. Bhide, J. Univ. Bombay, Seckt. A. 21, Pt. 3, 36 (1952); Ch. A. 48, 5135 (1954).

[16] A. Brunner, Analysis of azo dyes, State Chemical Press p. 92 (1933).*

[17] G. Charrier and G. Ferreri, Gazz. 41, II, 720 (1911).

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# REPLACEMENT OF HALOGEN IN AZO COMPOUNDS

## II. REACTION OF 2-CHLOROPHENYLAZO-2'-NAPHTHOL WITH PHENOLATES

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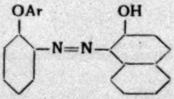
In the previous paper [1] we reported the replacement of a chlorine atom in o-chloro-o'-hydroxy azo dye by alkoxy groups. It was interesting to check the possibility of replacement of chlorine in this azo compound by aryloxy groups. The principal difference here consists of the fact that in this case the chlorine-containing dye is subjected to the action of an aqueous alkaline solution of a phenolate, i.e., conditions under which, according to Delfs [2, 3] there takes place a replacement of the chlorine atom by a hydroxy group with formation of a copper complex of the dihydroxy azo dye, rather than a reaction with an alcoholate in a practically anhydrous medium. It is interesting to note that in the examples in Delfs' patent relating to the replacement of chlorine in o-chloro-o'-hydroxy azo dyes by substituents other than the hydroxy group, the reaction with phenolates with formation of aryloxy derivatives is not described [4].

On heating under reflux at 100-110° 2-chlorophenylazo-2'-naphthol (the azo dye from 2-chloroaniline and 2-naphthol) with copper sulfate and an aqueous alkaline solution of phenol, o-, m- and p-cresols, 1,3,5- and 1,2,4-xylenols and with 4(1;1',3',3'-tetramethylbutyl)phenolate (p-iso-octylphenolate) in xylene medium there were obtained in high yields the products of replacement of the chlorine atom by the respective aryloxy groups, the yields in the majority of cases being quantitative. Thus there were prepared azo dyes which were derivatives of o-aminodiphenyl ether and its homologs.



where: Ar = $C_6H_5$, 2-$CH_3C_6H_4$, 3-$CH_3C_6H_4$, 4-$CH_3C_6H_4$, 3,5-$(CH_3)_2C_6H_3$, 2,4-$(CH_3)_2C_6H_3$ & 4-$(CH_3)_3CCH_2C(CH_3)_2C_6H_4$.

Control experiments in the absence of the copper salt gave negative results. In not a single case were there detected in the reaction mixture any noticeable amounts of the o,o'-dihydroxy azo dyes, i.e., the replacement of the chlorine atom by a hydroxyl group was not noted under the conditions used for the reaction (heating in aqueous alkaline medium in the presence of the copper salt).

The corresponding o-aryloxyanilines (homologs of o-aminodiphenyl ether) were prepared by reductive cleavage of some of these dyes. The dyes prepared by us were capable of dyeing acetate and polyamide fibers.

## EXPERIMENTAL*

Replacement of chlorine by phenoxy, 2-, 3- and 4-methylphenoxy and 3,5- and 2,4-dimethylphenoxy groups. Eight g of the azo dye from 2-chloroaniline and 2-naphthol (m.p. 167°; see [1]) triturated with 4 g of copper sulfate and 5 ml of water was introduced into the solution of the phenolate prepared by the reaction of 40 g of the appropriate phenol with 80 ml of 30% solution of sodium hydroxide. The mixture was heated under reflux with stirring for 8-12 hours at 100-110°, after which it was diluted with 2 volumes of water and the precipitate was filtered off. The precipitate was heated to boiling with 5% solution of sodium hydroxide, for the removal of excess phenol, was filtered again and washed with water; in case of necessity the washing with alkali was repeated. Then the precipitate was boiled with 100 ml of concentrated hydrochloric acid, was filtered off after dilution with water, washed free of chloride ions and dried in air. The test for chlorine was negative.

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* With participation by V. S. Zenkevich.

There was obtained 7.1 g (73.8%) of the phenoxy substituted dye. After recrystallization from glacial acetic acid it formed thin needles with m.p. 149°. According to the literature data [6]: m.p. 135°. The dye was soluble in toluene, ethyl alcohol and glacial acetic acid and insoluble in water.

Found %: C 77.57, 77.49; H 4.80, 4.89; N 8.39, 8.48. $C_{22}H_{16}O_2N_2$. Calculated %: C 77.65; H 4.70; N 8.23.

There was obtained 9.2 g (92%) of the 2-methylphenoxy substituted dye. After recrystallization from ethyl alcohol it formed narrow flat needles with m.p. 147.5-148.5°. The dye was readily soluble in benzene, toluene and chloroform, less readily in ethyl alcohol and very poorly soluble in glacial acetic acid (even on heating); it was insoluble in water.

Found %: C 78.0, 78.1; H 5.58, 5.65; N 7.88. $C_{26}H_{16}O_2N_2$. Calculated %: C 77.97; H 5.09; N 7.91.

There was obtained 9.7 g (96.8%) of the 3-methylphenoxy substituted dye. After recrystallization from ethyl alcohol it formed small flat needles with m.p. 115-116°. The dye was soluble in benzene, toluene, chloroform, carbon tetrachloride, glacial acetic acid and ethyl alcohol and insoluble in water. A solution in concentrated sulfuric acid had a red-violet color which changed to yellow after dilution of the solution with water.

Found %: C 77.87, 77.67; H 5.17, 5.00; N 8.05, 8.37. $C_{23}H_{18}O_2N_2$. Calculated %: C 77.97; H 5.09; N 7.91.

There was obtained 9.9 g (98.8%) of the 4-methylphenoxy substituted dye. After recrystallization from glacial acetic acid it formed wide flat needles with m.p. 165.5-166.5°.

The dye was soluble in benzene, toluene, chloroform, glacial acetic acid and ethyl alcohol and was insoluble in water.

Found %: C 77.73; 77.76; H 5.20, 5.13; N 8.01. $C_{23}H_{18}O_2N_2$. Calculated %: C 77.97; H 5.09; N 7.91.

There was obtained 9.4 g (90.2%) of the 3,5-dimethylphenoxy substituted dye. After recrystallization from ethyl alcohol it formed narrow sharp needles with m.p. 138.5-139°. The dye was soluble in chloroform, benzene, toluene, glacial acetic acid and ethyl alcohol and was insoluble in water. Its solution in concentrated sulfuric acid has a cherry red color which changed to yellow on dilution of the solution with water.

Found %: C 78.17, 78.04; H 5.55, 5.65; N 7.88. $C_{24}H_{20}O_2N_2$. Calculated %: C 78.26; H 5.43; N 7.61.

There was obtained 7.6 g (70.3%) of the 2,4-dimethylphenoxy substituted dye. After recrystallization from glacial acetic acid it formed long flat needles with m.p. 158.2-159°. The dye was soluble in benzene, toluene, acetone, chloroform, glacial acetic acid and ethyl alcohol and insoluble in water.

Found %: C 78.16, 78.0; H 5.53, 5.70; N 7.91, 8.00. $C_{24}H_{20}O_2N_2$. Calculated %: C 78.26; H 5.43; N 7.61.

Replacement of chlorine by 4(1',1',3',3'-tetramethylbutyl)phenoxy group (4-iso-octylphenoxy group). 3 g of the initial dye, triturated with 1.5 g of copper sulfate was introduced into the mixture of the iso-octylphenolate and xylene prepared by the reaction of 4.4 g of iso-octylphenol with 0.5 g of metallic sodium in 40 ml of xylene with heating. The resulting mixture was heated under reflux with stirring for 15 hours at 105-110°, after which the xylene was distilled in vacuum at 80°. The residue was boiled for 30 minutes with 50 ml of concentrated hydrochloric acid, washed with water, then with 5% solution of sodium hydroxide and again with water, after which it was dried in air. The weight was 4.75 g (98.9%). The test for chlorine was negative. After recrystallization from glacial acetic acid the dye was obtained in the form of bundles of long plates with uneven edges; m.p. 142.5-143°. The dye was readily soluble in the cold in benzene, toluene, xylene, chlorobenzene, chloroform and carbon tetrachloride; it was soluble with heating in ethyl alcohol, acetone and glacial acetic acid; it was insoluble in water.

Found %: C 79.60, 79.51; H 7.17, 7.23; N 6.29, 6.39. $C_{30}H_{32}O_2N_2$. Calculated %: C 79.64; H 7.08; N 6.19.

Preparation of 2(4'-methylphenoxy)aniline (2-amino-4'-methyldiphenyl ether). To the solution of stannous chloride prepared by the reaction of 2 g of metallic tin with 35 ml of concentrated hydrochloric acid with heating, there was added 35 ml of water and 1 g of 4-methylphenoxy substituted dye and the mixture was refluxed until it became colorless. The precipitate which formed on cooling was filtered off and was treated with 25 ml of 5% solution of sodium hydroxide with addition of 0.3 g of sodium hydrosulfite, after which the 2-(4'-methylphenoxy)aniline was extracted with ether. The ethereal layer was separated and treated with 2 ml of concentrated hydrochloric acid. After evaporation of ether from the residual aqueous layer there precipitated the hydrochloride salt of 2-(4'-methylphenoxy)aniline. Its weight was 0.47 g. After recrystallization from dilute methyl alcohol acidified by several drops of hydrochloric acid it formed flat needles with m.p. 187.5-189° (in sealed capillary). According to the literature data [15]: m.p. 220°.

Found %: C 66.60, 66.53; H 6.18, 6.09; N 6.05, 5.86. $C_{13}H_{14}ONCl$. Calculated %: C 66.24; H 5.94; N 5.94.

For preparation of the N-benzoyl derivative 0.1 g of the hydrochloride salt of 2-(4'-methylphenoxy)aniline was shaken with 2.5 ml of 20% solution of sodium hydroxide and 0.5 ml of benzoyl chloride after which the mixture was diluted with water and the precipitate was filtered off, washed and dried. Its weight was 0.11 g. After recrystallization from dilute methyl alcohol the benzoyl derivative was obtained in the form of bundles of colorless needles with m.p. 67-68°.

Found %: C 79.14, 78.96; H 5.80, 5.95; N 4.74. $C_{20}H_{17}O_2N$. Calculated %: C 79.20; H 5.61; N 4.62.

*Preparation of 2-(3',5'-dimethylphenoxy)aniline (2-amino-3',5'-dimethyldiphenyl ether).* The reductive cleavage of 3,5-dimethylphenoxy substituted dye was run as in the above case but the complete decolorization took place only after the reaction mixture had stood overnight and the precipitate of the hydrochloride salt of 2-(3',5'-dimethylphenoxy)aniline formed some 15 minutes after the addition of concentrated hydrochloric acid to the ethereal extract. The precipitate was filtered off, washed with a small volume of water, dried and recrystallized from methyl alcohol, after which it was obtained in the form of large colorless needles, with m.p. 186-188°.

Found %: C 67.11, 67.25; H 6.59, 6.49; N 5.72. $C_{14}H_{16}ONCl$. Calculated %: C 67.33; H 6.41; N 5.61.

For preparation of the N-benzoyl derivative 0.1 g of the hydrochloride of 2-(3',5'-dimethylphenoxy)aniline was benzoylated as described above. There was obtained 0.15 g of the benzoyl derivative which after recrystallization from methyl alcohol formed thin colorless needles with m.p. 139.5-140°.

Found %: C 79.44, 79.34; H 6.20, 6.08; N 4.22. $C_{21}H_{19}O_2N$. Calculated %: C 79.49; H 5.99; N 4.41.

*Preparation of 2-(2'-4'-dimethylphenoxy)aniline (2-amino-2',4'-dimethylphenyl ether).* The reductive cleavage was run as in previous cases. The hydrochloride salt of 2-(2'-4'-dimethylphenoxy)aniline was obtained, after recrystallization from dilute methyl alcohol, in the form of thin plates with m.p. 167-169°.

Found %: C 66.81, 66.89; H 6.88, 6.98; N 5.79, 5.71. $C_{14}H_{16}ONCl$. Calculated %: C 67.33; H 6.41; N 5.61.

We express our gratitude for valuable suggestions to N. N. Vorozhtsov.

## SUMMARY

1. The replacement of the chlorine atom by aryloxy groups with phenyl, 2-methylphenyl-, 3-methylphenyl, 4-methylphenyl, 3,5-dimethylphenyl, 2,4-dimethylphenyl and 4-(1',1',3',3'-tetramethylbutyl)phenyl (p-isooctylphenyl) residues was realized by the reaction of sodium phenolates with the azo dye from 2-chloroaniline and 2-naphthol.

2. It was shown that the replacement of chlorine in the given o-halo-o'-hydroxy azo dye by the aryloxy groups proceeds readily in aqueous alkaline medium in the presence of a copper salt and is not accompanied by any formation of noticeable amounts of the product of replacement of chlorine by the hydroxyl group.

3. Homologs of 2-aminodiphenyl ether (2-phenoxyaniline) with methyl groups in positions 4'-, 3',5'- and 2',4'- were prepared by reductive cleavage of the aryloxy substituted azo dyes.

## LITERATURE CITED

[1] B. I. Stepanov, M. A. Salivon, V. F. Lagidze and L. A. Dediukhina. J. Gen. Chem. 28, 1915 (1958).*

[2] German Patent 571,859; Friedlander 19, 1689.

[3] German Patent 738,900; Chem. Abstr. 39, 5502 (1945).

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*Original Russian pagination. See C. B. Translation.

[4] German Patent 658,841; Friedlander 24, 679.

[5] Beilst. 13, 360.

[6] Beilst. 16, E II, 73.

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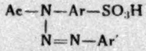
# REACTION OF DIAZO COMPOUNDS WITH SULFAMIC ACID AND ITS DERIVATIVES

## X. CONCERNING COLORED SALTS OF ACYLAMINOARYLSULFONIC ACIDS WITH DIAZONIUM BASES

D. Z. Zavel'skii and L. A. Lishnevskaia

In the previous papers [1, 2] we described the synthesis and the properties of arylsulfamates of diazonium compounds and discussed the reasons for their color. At that time a supposition was made that the cause for the color of these salts is the salt bond of a special character which carries the conjugation between the electron-acceptor system of the diazonium cation and the electron-donor system of the arylsulfamate anion.

There is an indication in the literature [3] that Schroeter had prepared the reaction products of diazonium salts with acylaminoarylsulfonic acids which turned out to be highly colored and quite stable. For example, acetylnaphthionic acid gave with 2-, 3- and 4-nitrophenyldiazonium compounds the correspondingly dark-red, light yellow-red and green-red crystals, while benzenesulfonylsulfanilic acid gave with the same diazonium compounds the orange-yellow, yellow and egg-yellow products. These substances turned out to be so stable that they readily underwent recrystallization from hot water. They evolved diazo nitrogen quantitatively on being boiled with water while on being heated in the dry state they ignited or charred. The author supposed at first, on the basis of the exceptional stability of these compounds, that they are diazoamino compounds [3] of type (I), but then characterized them as diazonium salts [4] of type (II) but failed to provide any information about their activity in diazo coupling reactions. For the products of reaction of 4-nitrophenyldiazonium compound with N-benzenesulfonyl substituted sulfanilic and naphthionic acids, Schroeter proposed the structure of acid azo dyes of type (III), since on being boiled with water they failed to evolve nitrogen and dyed wool from an acid bath.

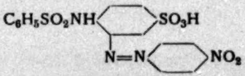


$$\begin{array}{l} Ac-N-Ar-SO_3H \\ \;\;\;\;\;\;| \\ \;\;\;\;\;N{=}N-Ar' \end{array}$$

(I)

$Ac-NH-Ar-SO_3-N_2Ar'$

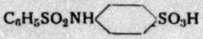
(II)

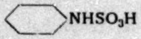


(III)

Three years later a patent was taken out [5] on the preparation of analogous products of reaction of diazonium chlorides with arylsulfamidoarylsulfonic acids which were named as diazoamino compounds in the patent. In later patents [6, 7] the same compounds were described as stable diazonium salts. Saunders [8] in discussing these contradictions in his well-known book gave Schroeter's compounds the structure of diazo salts.

The properties of Schroeter's compounds seemed to us, by description, to be so similar to diazonium arylsulfamates which had been studied by us, that we repeated Schroeter's work with the example of benzenesulfonylsulfanilic acid which is closest in its structure to arylsulfamic acids,





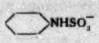
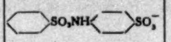
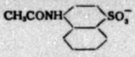
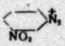
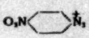
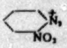
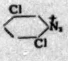
for the purpose of detailing the structure of these compounds and for a comparison of their properties, especially the color, with those of the diazonium arylsulfamates.

We synthesized benzenesulfonylsulfanilic acid, at first, by Schroeter's method [4], by dropwise introduction of benzenesulfonyl chloride into an aqueous solution of sodium sulfanilate which had been made alkaline; but, being convinced that this reaction does not proceed smoothly, we ran a condensation by trituration, without dilution by solvents, of a mixture of the two components at the temperature of a water bath. Here there was obtained a very pure benzenesulfonylsulfanilic acid in good yield.

By the action of the sodium salt of this acid on solutions of the chlorides of 2-nitro-, 3-nitro-, 4-nitro- and 2,5-dichlorophenyldiazonium compounds in mineral acids there were prepared four substances, of which three had been described by Schroeter while the fourth was prepared for the first time. The derivative of 2-nitrophenyldiazonium compound, after recrystallization from water, turned out to have an orange color, that from 3-nitrophenyldiazonium compound was light yellow, that from 4-nitrophenyldiazonium compound was egg-yellow, and that from 2,5-dichlorophenyldiazonium compound was lemon yellow. All these under the microscope showed the form of elongated plates. The products are poorly soluble in cold water, while 2-nitrophenyl derivative dissolved best in hot water, while 4-nitrophenyl derivative was less soluble, and the remaining two compounds were even less soluble. All these compounds, according to our experiments, couple quantitatively in neutral medium with azo components and are therefore true diazo salts. They lose the diazo nitrogen quantitatively on being boiled both in acid and in neutral media. In potentiometric titration they behave like true diazonium arylsulfonates since for the 4-nitrophenyldiazonium salt the isoelectric point lies at pH 5.9, while that for 2-nitrophenyldiazonium salt is at pH 4.8, and that for the sodium salt of benzenesulfonylsulfanilic acid is at pH 6.9. It should be noted that Schroeter's assertion to the effect that 4-nitrophenyldiazonium compound forms an azo dye with benzenesulfonylsulfanilic acid, and not a diazonium salt, is evidently based on a misunderstanding.

The table illustrates the dependence of the color of the diazonium salt on the anion of arylsulfamido- or acylaminoarylsulfonic acid which enters its composition.

Dependence of Color of Diazonium Salt on Anion Structure

| Diazo cation | Structure of the anion and color of the salt | | |
|---|---|---|---|
| |  |  |  |
|  | Orange | Light yellow | Light yellow-red |
|  | Dark red-brown | Egg-yellow | Greenish-red |
|  | Very dark<br>(red-brown)<br>(very soluble) | Orange | Dark red |
|  | Bright red | Lemon yellow | |

From the data in the table it is possible to make the following observations.

1) The benzenesulfonylsulfanilates are considerably more colored than are the analogous arylsulfamates. The cause for the hypsochromic effect is evidently the fact that between the amino and the sulfo groups in benzenesulfonylsulfanilates there is located a phenyl nucleus and that the amino group is replaced by the electrophilic acyl residue.

2) Diazonium acetylnaphthionates are more deeply colored than are the corresponding benzenesulfonylsulfanilates. This bathochromic effect must be explained by the decrease of acidity of the acyl substituent in the amino group and replacement of the phenyl nucleus by naphthalene.

3) In all three series of the colored diazonium salts it is clearly evident that their color deepens within each series from 3-nitro, through 4-nitro, to the 2-nitro derivative, i.e., according to the growth of the electrophilic nature of the nitro group depending on its position in the benzene nucleus.

## EXPERIMENTAL

Synthesis of benzenesulfonylsulfanilic acid $C_6H_5SO_2NHC_6H_4SO_3H$. Four g of the sodium salt of sulfanilic acid was triturated in a porcelain dish with 5 g of benzenesulfonyl chloride and was gently heated on a sand bath with energetic rubbing. The precipitate, which at first liquefied, then gradually thickened to a solid paste was transferred to a beaker and was stirred with 30 ml of water heated to 72°. The main bulk of the precipitate went into solution. The solution was filtered from the small amount of a white precipitate, chilled in ice and treated with an excess of sulfuric acid. A colorless crystalline precipitate formed immediately. The precipitate was filtered off after chilling with ice; it was then washed with ice water and dried.

Found %: S 19.9. $C_{12}H_{11}O_5NS_2$. Calculated %: S 20.46.

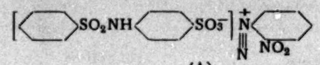
In the potentiometric titration of the benzenesulfonylsulfanilic acid with alkali, its point of equivalence was found at pH 6.9.

Preparation of solutions of the diazo compounds. The arylamine (0.01 mole) was mixed with 6 ml of 5 N hydrochloric acid and stirred for 30 minutes at room temperature, then treated with 7 g of powdered ice whereby the temperature declined to −6°. To this reaction mixture there was added in one portion 2.1 ml of 5 N solution of sodium nitrite. The temperature rose to 6-8° and, after a few minutes, the solution became almost transparent. It was filtered and treated with a few drops of a solution of sulfamic acid for destruction of the excess nitrous acid, controlling the reaction with a test paper dyed with Metanil yellow.

In case of o-nitro- or 2,5-dichloroanilines the amount of the acid was increased to 10 ml and that of nitrite to 2.2 ml.

Reaction of benzenesulfonylsulfanilic acid with diazonium chlorides. Benzenesulfonylsulfanilic acid (0.01 mole) was dissolved in a slight excess of concentrated soda solution. The excess soda was eliminated by addition of acetic acid. To the solution, chilled with ice, there was added with stirring the solution of the diazonium compound prepared from 0.01 mole of amine.

2-Nitrophenyldiazonium salt of benzenesulfonylsulfanilic acid (A). On addition of the diazonium solution into the sulfonate solution there formed immediately a thick yellow-orange precipitate. This was filtered off, washed with cold water and recrystallized from water heated to 65-70°. There were obtained crystals with orange color with a golden sheen. Under a microscope they appeared as elongated plates.



(A)

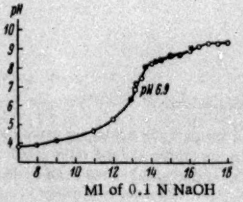


Fig. 1. Potentiometric titration of benzenesulfonylsulfanilic acid.

A solution or a suspension of the substance in water couples intensively with azo dye components. The product is readily soluble, with yellow color, in solutions of sodium hydroxide. A red solution is formed with 20% solution of ammonia, this solution yielding a red precipitate. The substance does not contain sodium (ash).

Analysis for diazo nitrogen content:

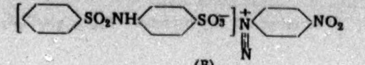
a) Decomposition in 50% sulfuric acid. Found %: diazo nitrogen 6.28. $C_{18}H_{14}O_7N_4S_2$. Calculated %: diazo nitrogen 6.07.

b) Decomposition in boiling water. Found %: diazo nitrogen 5.85. $C_{18}H_{14}O_7N_4S_2$. Calculated %: diazo nitrogen 6.07.

Determination of the diazo component. A sample of the substance was suspended in 150-200 ml of water. To this suspension there was added with good stirring an excess of 0.1 N alkaline solution of β-naphthol, which had been adjusted to pH 7 by addition of acetic acid. After 30-40 minutes stirring the excess β-naphthol was titrated with 4-nitrophenyldiazonium solution. 0.5605 g of substance taken: 12.34 ml of 0.1 N β-naphthol. $C_{18}H_{14}O_7N_4S_2$. Calculated: 12.12 ml of 0.1 N β-naphthol.

In the potentiometric titration of the diazonium salt in aqueous solution with 0.1 N solution of sodium hydroxide the point of equivalence was found to lie at pH 4.

4-Nitrophenyldiazonium salt of benzenesulfonylsulfanilic acid (B). To a concentrated solution



(B)

of the arylsulfonate there was added the diazonium solution. A thick yellow precipitate formed immediately. This was filtered off, washed with cold water and pressed on a porous plate. The diazonium salt was sparingly soluble in cold water, more readily soluble in hot water with formation of a yellowish solution.

No gas evolution was observed on the heating of the aqueous solution to 75°. The diazonium salts coupled energetically with azo dye components. After recrystallization from water at 75° there were obtained, after chilling with ice, the egg-yellow large shiny crystals of the product. Under a microscope these appear as elongated plates.

The substance dissolved in sodium hydroxide with red coloration. In ammonium hydroxide it also gave a red colored solution from which there formed a red-brown precipitate.

Analysis for diazo nitrogen:

Found %: diazo nitrogen 6.23, 6.28. $C_{18}H_{14}O_7N_4S_2$. Calculated %: diazo nitrogen 6.07.

Determination of diazo component (coupling with β-naphthol):

0.6286 g of the substance: 13.5 ml of 0.1 N β-naphthol. $C_{18}H_{14}O_7N_4S_2$. Calculated : 13.59 ml of 0.1 N β-naphthol.

The isoelectric point was found to be at pH 5.9, in the potentiometric titration of the diazo salt with 0.1 N solution of hydrochloric acid with a glass electrode.

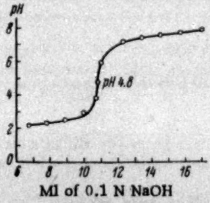


Fig. 2. Potentiometric titration of 2-nitrophenyldiazonium salt of benzenesulfonylsulfanilic acid.

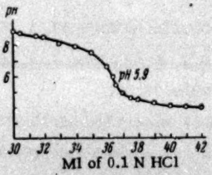
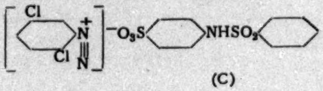


Fig. 3. Potentiometric titration of 4-nitrophenyldiazonium salt of benzenesulfonylsulfanilic acid.

2,5-Dichlorophenyldiazonium salt of benzenesulfonylsulfanilic acid (C). On pouring the diazonium solution into the suspension of benzenesulfonylsulfanilic acid, the reaction mixture crystallized to a thick mass of crystals with lemon yellow color. These appeared as plates under a microscope.



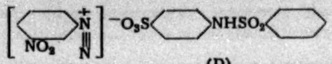
(C)

The precipitate, after filtration, washing and drying, was very slightly soluble in cold water and somewhat more soluble in hot water. The product couples intensively with azo dye components. It dissolved completely with a yellow-orange color in a solution of sodium hydroxide.

Analysis for the content of the diazo component (coupling with β-naphthol):

0.7426 g of product: 14.92 ml of 0.1 N β-naphthol. $C_{18}H_{13}O_5N_3Cl_2S_2$. Calculated: 15.27 ml of 0.1 N β-naphthol.

3-Nitrophenyldiazonium salt of benzenesulfonylsulfanilic acid (D). On mixing the solutions of 3-nitrophenyldiazonium salt and sodium acylsulfanilate there formed immediately a thick yellow precipitate. Under the microscope these appeared as slightly yellow plates. The substance was poorly soluble in cold water and somewhat more soluble in hot water. It coupled intensively with azo dye components and formed a yellow solution with sodium hydroxide.



(D)

## SUMMARY

1. It was shown that the colored reaction products of diazonium salts with acylaminoarylsulfonic acids, which had been synthesized by Schroeter, are true diazonium salts.

2. It was found that diazonium acylaminoarylsulfonates are colored more deeply when the substituents in the aryl nucleus of the diazonium portion are more electrophilic, when the acid character of the acyl group is less pronounced and when a greater number of condensed benzene nuclei are contained in the aryl group of the acylaminoarylsulfonic acid.

3. It was suggested that the reason for the color of the diazonium acylaminoarylsulfonates, as for diazonium arylsulfamates, is the special salt bond between the ions of these salts, which is aided by conjugation between the electron-donor system of the anion and the electrophilic system of the cation.

## LITERATURE CITED

[1] D. Z. Zavel'skii and L. A. Lishnevskaia, J. Gen. Chem. 28, 755 (1958).*

[2] D. Z. Zavel'skii and L. A. Lishnevskaia, J. Gen. Chem. 28, 1010 (1958).*

[3] Beilst, 16, 491.

[4] G. Schroeter, Ber. 39, 1559 (1906).

[5] German Patent 229,247 (1909); Friedlander 10, 786.

[6] Swiss Patent 166,218; German Patent 593,260 (1932); Friedlander 20, 1227 (1933).

[7] French Patent 735,865 (1932); Chem. Zentr. 1933, II, 3347.

[8] K. Saunders, Aromatic diazo compounds and their technological use, State Scientific and Technical Press, p. 217 (1938). **

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*Original Russian pagination. See C. B. Translation.

** Russian translation.

# SYNTHESES OF VINYL MONOMERS

## III. CONCERNING THE SYNTHESES OF VINYL ESTERS FROM ACETO- AND CHLOROMERCURIACETALDEHYDES AND CONCERNING THE MECHANISM OF THESE REACTIONS

A. Ia. Iakubovich, V. V. Razumovskii, Z. N. Vostrukhina
and S. M. Rozenshtein

We decided to use, for the preparation of some vinyl esters, the method of their synthesis that had been described recently by A. M. Sladkov and G. S. Petrov [1]. This method consists of the reaction of acetaldehyde with the chloride of the appropriate acid in the medium of a tertiary base and leads, according to the data given by the authors, to the formation of vinyl ester in yields up to 90% of theoretical.

Working with pyridine we attempted at first to prepare in this manner some vinyl benzoate, using the conditions indicated by the authors to be the optimum ones (yield of ester 83%). However we failed to prepare this ester. Similarly fruitless were the attempts to prepare vinyl acetate by this method. Owing to the briefness of the description of the technique in the cited article, we turned to Sladkov's dissertation [2] and tried to prepare vinyl esters of butyric, caproic and chloroacetic acids, using the detailed directions given in this dissertation. However, none of these esters could be prepared by us, working with pyridine.

It is proper to note here that in the cited publications there are not given any indications that on mixing of pyridine, acetaldehyde and an acyl chloride there occurs an abundant formation of crystalline precipitates; more will be said below about the nature of these compounds.

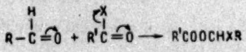
Vinyl esters of acids of phosphorus may be prepared by the reaction of acetaldehyde with chlorides of such acids in the presence of triethylamine [3]. We made an attempt to prepare some vinyl benzoate with replacement of pyridine by triethylamine. In this case there was obtained some vinyl benzoate in a yield about 15% of theoretical.

Considering the above, we turned to the synthesis of vinyl esters by another method [4]. We prepared by this method in satisfactory yields the vinyl esters of benzoic, p-cyanobenzoic, trifluoroacetic and other acids.

A. N. Nesmeianov and I. F. Lutsenko [5] regard the reactions of monochloromercuriacetaldehyde with acyl chlorides, which leads to the formation of vinyl esters, as reactions with a transfer of the reactive center.

On the basis of material given below it seems to us that such a concept is debatable. In their discussion of the reaction mechanism, Nesmeianov and Lutsenko start with the supposition that carbonyl compounds enter the reactions with acylating agents only with difficulty and that the appearance of a well defined reactivity of the carbonyl group in chloromercuriacetaldehyde in respect to acyl halides is ascribed almost completely to the σ,π-conjugation of the Hg−C and C=O bonds.

However, in reality the carbonyl group of aldehydes in the absence of a conjugated Hg−C bond remains still quite reactive in respect to acyl halides, as will be clear from the data shown below. Actually, according to the data from a number of workers [6-10], benzaldehyde and its derivatives readily add halides of aliphatic and aromatic acids with formation of esters by the reaction scheme:



$$R-\overset{H}{\overset{|}{C}}=O + R'\overset{X}{\overset{|}{C}}=O \longrightarrow R'COOCHXR$$

Formaldehyde also reacts analogously as has been shown by many examples [11, 12] and confirmed in the present work by the syntheses of chloro- and bromomethyl methacrylates from paraformaldehyde and corresponding halides of methacrylic acid.

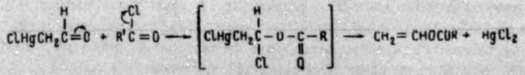
Evidently, the activity of the carbonyl group in formaldehyde is sufficiently great despite the absence of $\pi,\pi$-conjugation of the carbonyl group bond, as it exists in the analogously reacting benzaldehyde and cinnamaldehyde, and the addition of acyl halides to it proceeds easily. However, formaldehyde is not an exception. Acetaldehyde, as established by us in an example with acetyl chloride, is capable of combining with it on simple mixing at normal temperature with heat evolution, forming $\alpha$-chloroethyl acetate thereby. In the presence of traces of zinc chloride which catalyzes the addition, the reaction proceeds violently.

We prepared the previously undescribed $\alpha$-chloroethyl methacrylate by the reaction of acetaldehyde with the chloride of methacrylic acid in the presence of zinc chloride. A similar addition has been observed previously [13-16] in heating of a mixture of acetaldehyde or its homologs with acyl chlorides in a sealed tube at 100°. Thus, it is quite clear that the readily proceeding addition of acyl chlorides to aldehydes with formation of $\alpha$-halogenated alkyl or aralkyl esters of carboxylic acids is a general reaction.*

There is hardly an basis to think that in the case of chloromercuriacetaldehyde its reaction with acyl halides must proceed by another route and to speak in this case about the transfer of the reactive center [18].

The "dual" reactivity of chloromercuriacetaldehyde in respect to acyl halides (incidentally, one never observed thus far) or to compounds analogous to them (triphenylhalomethanes) may arise, evidently owing to the fact that this aldehyde is a bifunctional compound.

Whether the reaction of chloromercuriacetaldehyde with acyl halides yields vinyl esters of the result of elimination of mercuric chloride in two stages, i.e., as a 1-2 addition according to the scheme:



$$\mathrm{ClHgCH_2}\overset{\mathrm{H}}{\overset{|}{\mathrm{C}}}{=}\mathrm{O} + \mathrm{R'}\overset{\mathrm{Cl}}{\overset{|}{\mathrm{C}}}{=}\mathrm{O} \longrightarrow \left[\mathrm{ClHgCH_2}\underset{\mathrm{Cl}}{\underset{|}{\overset{\mathrm{H}}{\overset{|}{\mathrm{C}}}}}-\mathrm{O}-\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}-\mathrm{R}\right] \longrightarrow \mathrm{CH_2{=}CHOCOR} + \mathrm{HgCl_2}$$

or whether the entire reaction proceeds in one act (1-4 addition), is not strictly proven at this time. However, all the material shown above and below about the reactions of aldehydes with acyl halides permits one to allow that the reaction may proceed in two stages; here as the result of the addition of acyl halide to chloromercuriacetaldehyde there arises an unstable $\beta$-chloromercuric chloride which, by losing mercuric chloride, is transformed into the vinyl ester. This possibility is confirmed by some degree by the material shown below.

We isolated and examined the crystalline compounds formed in the reaction of acetaldehyde and pyridine with benzoyl chloride and acetyl chloride. Their examination showed that they are adducts of the composition $(C_5H_5NRCOClCH_3CHO)_2$. By their behavior and properties these compounds are salt-like substances.

The same compounds could be prepared by the reaction of pyridine with $\alpha$-chloroethyl benzoate and $\alpha$-chloroethyl acetate, respectively:

$$\mathrm{RCO_2CHClCH_3 + C_5H_5N \longrightarrow \underset{(I)}{[C_5H_5NCH(CH_3)(O_2CR)]Cl}}$$

Thus it appears evident that the adducts are salts of quaternary bases, i.e., chlorides of $\alpha$-acyl(aroyl)hydroxyethylpyridinium ion (I) (also see [10]).

We also found that in the reaction of acetaldehyde, benzoyl chloride and triethyl amine there is formed in 15% yield some vinyl benzoate. One can hardly doubt that in this reaction, as well, there occurs the intermediate formation of a quaternary salt which is analogous to those shown above. However this salt, being less stable thermally than the corresponding pyridinium salt, decomposes already at room temperature, forming thereby the vinyl benzoate along with other substances:

$$\mathrm{(C_2H_5)_3N + C_6H_5COCl \longrightarrow (C_2H_5)_3NC_6H_5COCl \xrightarrow{CH_3CHO}}$$
$$\mathrm{\longrightarrow [(C_2H_5)_3NCH(CH_3)(O_2CC_6H_5)]Cl \longrightarrow (C_2H_5)_3NHCl + CH_2{=}CHOCOC_6H_5}$$

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* Formation of analogous esters in the reaction of aldehydes with chlorides of acids of phosphorus has been noted by M. I. Kabachnik and E. S. Shepeleva [17].

This concept of the course of this reaction is confirmed by the results of the thermal decomposition of the chloride of α-benzoxyethylpyridinium ion, studied by us. The substance decomposes at 185-190°, forming vinyl benzoate in about 20% yield.*

If the above shown scheme for the formation of vinyl ester from acetaldehyde and an acyl chloride in triethylamine medium correctly shows the reaction mechanism for this reaction, as one may admit from all the material discussed above, then one should consider that the nature of the origin of vinyl ester groupings in this reaction and in the Nesmeianov reaction is common to each other. In one case there occurs an α,β-dehydrohalogenation of α-chloroethyl ester as the result of a Hoffman decomposition of the quaternary ammonium salt, while in the other case there occurs a α,β-dechloromercuration of a β-mercury substituted α-chloroethyl ester of the acid.

## EXPERIMENTAL

### I. Addition Reactions of Acyl Halides to Aldehydes

Preparation of chloromethyl methacrylate. To a mixture of 52.3 g of methacrylyl chloride and 15 g of paraformaldehyde there was added a 60-65° 1.5 g of anhydrous zinc chloride; the mixture began to boil. After clarification, the mixture was distilled in vacuum and the fraction at 70-110° at 15 mm was collected. The distillate was kept for two days over fused potassium carbonate and was then fractionated. There was obtained 25.1 g (36%) of chloromethyl methacrylate:

B.p. 63-65° at 62 mm, $d^{20}_4$ 1.1346, $n^{20}D$ 1.1449**, $MR_D$ 31.5; calculated 31.3.
Found %: C 44.70; H 5.25; Cl 25.53. $C_5H_7O_2Cl$. Calculated %: C 44.6; H 5.20; Cl 26.3.

Preparation of bromomethyl methacrylate. After termination of the reaction of 75 g of methacrylyl bromide and 15 g of paraformaldehyde (2.0 g anhydrous zinc chloride) under the conditions of the previous experiment, the filtrate was freed of unreacted bromide by means of a benzene solution of aniline (20 g of aniline in 150 ml). The precipitate was filtered off and the filtrate was washed with 3% hydrochloric acid, and with water, then was dried and distilled in the presence of cuprous chloride; there was collected a fraction with b.p. 60-90° at 50 mm (58 g). After a second fractionation there was isolated 32 g (35.8%) of bromomethyl methacrylate:

B.p. 85-86° at 50 mm, $d^{20}_4$ 1.4173, $n^{20}D$ 1.4690, $MR_D$ 34.6; calculated 34.24.
Found %: C 33.41; H 3.66; Br 44.52. $C_5H_7O_2Br$. Calculated %: C 33.5; H 3.9; Br 44.7.

Preparation of α-chloroethyl acetate. To 46 g of acetyl chloride there was rapidly added 35 g of acetaldehyde (heating of the mixture was observed) and the mixture was stirred for three hours. After distillation there were collected two fractions: 40-100° (37.3 g) and 101-125° (42.5 g). After a second distillation there was obtained 32.2 g of the α-chloroethyl acetate for 43.8% yield, from the fraction 101-125°.

B.p. 120-124°, $d^{20}_4$ 1.108, $n^{20}D$ 1.4080 (according to data of [19]: b.p. 120-124°).
Found %: Cl 28.8. $C_4H_7O_2Cl$. Calculated %: Cl 28.9.

Preparation of α-chloroethyl methacrylate. To the mixture of 104 g of methacrylyl chloride and 52 g of acetaldehyde preheated to 40° there was added a pair of small pieces of anhydrous zinc chloride (violent reaction). The mixture was stirred for one hour at 50° with 0.1 g of cuprous chloride. Two fractions were collected on distillation: 40-45° at 3 mm, 109 g, and 46-70° at 3 mm, 12 g. On second distillation of the first fraction there was isolated 105 g of α-chloroethyl methacrylate (70.7%).

B.p. 41-42° at 3 mm, $d^{20}_4$ 1.0801, $n^{20}D$ 1.4386, $MR_D$ 36.14; calculated 35.96.
Found %: C 49.48, 49.63; H 6.97, 6.87; Cl 24.32. $C_6H_9O_2Cl$. Calculated %: C 48.5; H 6.1; Cl 23.9.

Preparation of α-chloroethyl benzoate. To the mixture of 140 g of benzoyl chloride and 80 g of acetaldehyde there was added 0.1 g of anhydrous zinc chloride (energetic reaction). The mixture, heated to 70-75°, was kept for 1 hour; then 150 ml of ether was added and the solution was washed with 10% solution of sodium carbonate. After the usual treatment and triple distillation of the product there was obtained 77.5 g (42%) of α-chloroethyl benzoate:

B.p. 97-98° at 1 mm, $d^{20}_4$ 1.172, $n^{20}D$ 1.5171. According to data of [16]: b.p. 120° at 8 mm.

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* An analogous conception of the mechanism of formation of vinyl esters in the reaction of acetaldehyde, chlorides of acids and phosphorus and tertiary bases, was expressed by Gefter [3].

** As in original — Publisher's note.

Found %: Cl 19.1. $C_9H_9O_2Cl$. Calculated %: Cl 19.2.

## II. Reaction of Acetaldehyde With Halides of Acids in the Presence of Tertiary Bases

Acetaldehyde of acyl chlorides were used in the freshly distilled state. Pyridine was dried over potassium hydroxide and was then distilled from barium oxide, the fraction 115.5-116.1° being collected.

Preparation of α-benzoxyethylpyridinium chloride. a) To the solution of 27 g of acetaldehyde in 95 g of pyridine there was added over 2.5 hours at −10° to −12° with stirring 42 g of benzoyl chloride, during which the formation of a crystalline precipitate was observed.

The precipitate was filtered off and washed with dry ether. The yield was 76 g (96.3%, calculated on benzoyl chloride). The substance is readily soluble in water and the solution gives a test for chloride ion. It is soluble in alcohol, chloroform and glacial acetic acid and insoluble in ether and benzene. It was recrystallized from alcohol by addition of four volumes of ether; it formed colorless needles melting with decomposition at 179-180°.

Found %: C 63.80, 63.60; H 5.04, 5.22; N 5.16, 5.22; Cl 13.28, 13.32. M 532.5 (cryoscopic; acetic acid), 534.0 (ebullioscopic; chloroform). $(C_{14}H_{14}O_2NCl)_2$. Calculated %: C 63.75; H 5.31; N 5.31; Cl 13.43. M 527.

b) A mixture of 23 g of α-chloroethyl benzoate and 12 g of dry pyridine was heated for five hours at 80°. On the following day the upper liquid layer was decanted and the resulting glassy resinous product was washed three times with dry ether. On rubbing with a glass rod, the product crystallized. The yield was 5.7 g. On the following day, from the reaction liquid there separated 2.3 g of additional crystals of the same product. The substance was recrystallized from alcohol by precipitation with ether; it formed colorless crystals which decomposed at 173-175°.

Found %: C 62.94, 62.83; H 5.55, 5.83; N 4.58, 4.78; Cl 13.9, 13.5. $C_{14}H_{14}O_2NCl$. Calculated %: C 63.75; H 5.31; Cl 13.43; N 5.31.

Preparation of α-acetoxyethylpyridinium chloride. a) To a mixture of 55 g of pyridine and 13.5 g of acetaldehyde there was added a 0° with stirring 11.7 g of acetyl chloride, the addition being made gradually; formation of a precipitate began shortly. After heating the mixture to 80° the further treatment was as in the previous experiment. The yield was 35 g (83.3%, calculated on acetyl chloride). The substance dissolves in water, alcohol and chloroform and is insoluble in ether. It was recrystallized from alcohol by precipitation with ether. Colorless crystals with m.p. 140-150° (with decomposition).

Found %: C 52.36, 52.50; H 7.25, 7.40; N 7.61, 7.73. $C_9H_{12}O_2NCl$. Calculated %: C 53.20; H 6.0; N 6.95.

b) A mixture of 40 g of pyridine and 19 g of α-chloroethyl acetate was stirred for five hours while the temperature was gradually raised to 80°. The resulting precipitate was filtered off, washed with absolute ether and dried. The yield was 28.5 g (54%). The substance was recrystallized from alcohol by precipitation with ether; colorless needles with m.p. 140-150° (with decomposition).

Found %: C 53.64; H 6.5; N 7.17; Cl 18.67. $C_9H_{12}O_2NCl$. Calculated %: C 53.2; H 6.0; N 6.95; Cl 17.6.

Preparation of vinyl benzoate. a) To 81 g of triethylamine there was added a mixture of 28 g of benzoyl chloride and 17.6 g of acetaldehyde. The mixture was stirred for four hours at room temperature and stood for 48 hours. The resulting precipitate of triethylamine hydrochloride was separated. After two distillations of the filtrate there was isolated 12 g of a liquid with b.p. 51-53° at 2-3 mm which was not separated by further fractionation. According to chlorine analysis this liquid contained 32% of benzoyl chloride. To the solution of 10 g of this liquid in 75 ml of benzene there was added, for the separation of benzoyl chloride, gradually 4.6 g of aniline in 75 ml of benzene. The precipitate of benzanilide (7.1 g) was filtered off. The filtrate was washed with 0.5 N sulfuric acid and water, dried and subjected to vacuum distillation. There was isolated 4 g (16% on benzoyl chloride) and vinyl benzoate with b.p. 63-63° at 2-3 mm, $d^{20}_4$ 1.0670, $n^{20}D$ 1.5270.

A specially prepared mixture of vinyl benzoate and benzoyl chloride in 2 : 1 weight ratio boiled without separation at 50° at 2-3 mm.

b) 26.5 g of α-benzoxyethylpyridinium chloride was heated in a flask at 1-2 mm pressure on an oil bath at

187-190°. In a trap which was cooled with dry ice there was collected 0.5 g of a liquid, on the distillation of which there were detected pyridine and acetaldehyde. In the receiver after the trap, there was collected 6.5 g of a liquid. An ethereal solution of this liquid was washed with 0.5 N solution of hydrochloric acid, and with water; after drying it was distilled yielding 3.3 g (20%) of vinyl benzoate with b.p. 80-81° at 6-7 mm, $n^{20}D$ 1.5260.

## III. Syntheses of Vinyl Esters by the Nesmianov Method

*Preparation of vinyl p-cyanobenzoate* was run by the technique which was described for vinyl p-nitrobenzoate [4].

From 12.5 g of chloromercuriacetaldehyde and 6.5 g of p-cyanobenzoyl chloride there was obtained 5.2 g of a crystalline substance with m.p. 46-47°. After recrystallization from anhydrous alcohol (10 g of alcohol per 1 g of product) with chilling of the solution to −70° there was obtained 3.5 g (50%) of vinyl p-cyanobenzoate with m.p. 44-45°.

Found %: C 68.64, 68.51; H 4.57, 4.75; N 7.79, 8.17. $C_{10}H_7O_2N$. Calculated %: C 69.36; H 4.04; N 8.09.

*Preparation of vinyl trifluoroacetate.* Into a mixture of 35 ml of dry xylene and 28 g of monochloromercuriacetaldehyde there was passed with stirring at 4-5° 10 g of trifluoroacetyl chloride over five hours. Then the mixture was stirred for one hour at room temperature and allowed to stand until the next day. The precipitate was filtered off and the reaction product was distilled from the solution of 50° at pressure of 30 mm, the product being collected in a receiver cooled with a mixture of dry ice and acetone. The distillate (6 g) was kept for three days over solid sodium bicarbonate and was then distilled. After a second distillation there was collected 4.5 g (32%) of vinyl trifluoroacetate with b.p. 40-41°, $n^{25}D$ 1.3210. According to patents [20]: b.p. 37-39° and 40.5°, $n^{24}D$ 1.3162, and $n^{25}D$ 1.3151.

## SUMMARY

1. It was impossible to reproduce the synthesis of a series of vinyl esters of carboxylic acids from acetaldehyde, acyl chlorides and pyridine. In these reactions there were isolated the α-acyloxyalkylpyridinium chlorides, which were stable compounds. Vinyl benzoate was obtained in 15% yield of the theoretical after replacement of pyridine by triethylamine in the reaction with benzoyl chloride.

2. By direct addition of acyl halides to aldehydes there were synthesized α-chloroethyl acetate, α-chloroethyl benzoate, chloromethyl methacrylate, bromomethyl methacrylate and α-chloroethyl methacrylate. The reaction of addition of acyl halides to aldehydes is a completely general one and deserves mention in manuals on organic chemistry along with other typical reactions of addition among aldehydes.

3. By means of Nesmeianov reaction (Nesmeianov and co-workers) – reaction of monochloromercuriacetaldehyde with acyl halides – there were synthesized vinyl trifluoroacetate and vinyl p-cyanobenzoate.

The chemistry of the Nesmeianov reaction and the reaction of formation of vinyl benzoate from acetaldehyde and benzoyl chloride were discussed.

## LITERATURE CITED

[1] A. M. Sladkov and G. S. Petrov, J. Gen. Chem. 24, 450 (1954).*

[2] A. M. Sladkov, Dissertation "A study in the field of synthesis of vinyl esters," Moscow (1950).**

[3] E. L. Gefter, Dissertation "About synthesis and a study of some vinyl esters of acids of phosphorus," Moscow (1954).**

[4] A. N. Nesmeianov, I. F. Lutsenko and Z. M. Tumanova, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1949, 601; Scientific Notes of Moscow State University, No. 132, organic chemistry, book 7, 44 (1950); A. N. Nesmeianov and E. G. Perevalov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1954, 1002.*

[5] A. N. Nesmeianov and I. F. Lutsenko, Doklady Akad. Nauk SSSR 59, 707 (1948); also see: A. N. Nesmeianov and M. I. Kabachnik, J. Gen. Chem. 25, 41 (1955).*

---

*Original Russian pagination. See C. B. Translation.

**In Russian.

[6] H. Staudinger and E. Anthes, Ber. 46, 1417 (1913).

[7] H. Staudinger and E. Anthes, Ber. 46, 1426 (1913).

[8] H. Staudinger, Ber. 42 3966 (1909).

[9] R. Adams and E. Vollweiler, J. Am. Chem. Soc. 40, 1732 (1918).

[10] H. French and R. Adams, J. Am. Chem. Soc. 43, 650 (1921).

[11] L. Henry, Bull. Acad. roy. Belg. 1900, 48.

[12] M. Descude, Bull. Soc. Chim. (3) 27, 867 (1902); Ann. Chim. (7) 29, 486 (1903).

[13] M. Simpson, Lieb. Ann. 109, 156 (1859).

[14] R. Schiff, Ber. 9, 304 (1876).

[15] R. Rübencamp, Lieb. Ann. 225, 267 (1884).

[16] L. H. Ulich and R. Adams, J. Am. Chem. Soc. 43, 660 (1921).

[17] M. I. Kabachnik and E. S. Shepeleva, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1953, 682.*

[18] Chichibabin, Basic principles of organic chemistry, State Chemical Press, p. 137 (1953).**

[19] K. Freudenberg, and D. Peters, Ber. 52, 1463 (1919); S. I. Lur'e, J. Gen. Chem. 18, 1517 (1948); H. Adkins and B. Thompson, J. Am. Chem. Soc. 71, 2242 (1949).

[20] U. S. Patent 2,236,144 and 2,525,526; Chem. Abstr. 42, 3216 (1948) and 45, 1619 (1951).

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** Original Russian pagination. See C. B. Translation.

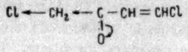
* In Russian.

# A STUDY IN THE ISOXAZOLE SERIES

## VI. CONCERNING THE SYNTHESIS OF 3-SUBSTITUTED ISOXAZOLES

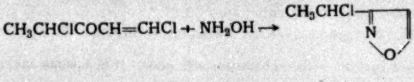
N. K. Kochetkov and A. Ia. Khorlin

One of the simplest methods of synthesis of isoxazole – the reaction of β-chlorovinyl ketones with hydroxylamine – has been studied in detail in our laboratory [1, 2]. A material fault of this method is the formation of a mixture of approximately equal amounts of isomeric 3- and 5-substituted isoxazoles, which fact is due to the two competing processes – the nucleophilic attack of hydroxylamine at the oxygen of the carbonyl group or at the β-carbon atom with replacement of the chlorine atom [1]. It was later shown by one of us [3] that β-dialkylaminovinyl ketones react with hydroxylamine in a practically singular manner, forming almost pure 5-substituted isoxazoles; in this case the attack of hydroxylamine is directed to the β-carbon atom owing to the suppression of the electrophilic activity of the carbonyl group. Finally it was shown [1] that chloromethyl β-chlorovinyl ketone reacts and forms 3-chloromethylisoxazole. This latter circumstance indicates that in this case the nucleophilic attack by hydroxylamine is directed solely at the carbonyl group, which is distinguished by an enhanced electrophilicity, evidently owing to the additional inductive effect produced by the halogen atom in α'-position.

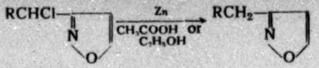


For checking this supposition we decided to establish whether or not such an effect of the halogen atom is general for the α'-position of the alkyl radical of alkyl β-chlorovinyl ketones and, with this purpose in mind, we studied the reaction of α'-chloroethyl β-chlorovinyl ketone with hydroxylamine.

Only chloromethyl β-chlorovinyl ketone and β'-chloroethyl β-chlorovinyl ketone are known at this time among alkyl β-chlorovinyl ketones which have substituents in the alkyl radical. It turned out that the synthesis of α'-chloroethyl β-chlorovinyl ketone also does not present any difficulties and is readily performed by the general method of synthesis of alkyl β-chlorovinyl ketones developed in our laboratory [4]. In the condensation of α'-chloroethyl β-chlorovinyl ketone with hydroxylamine in methanol there was obtained, in good yield, α'-chloroethyl isoxazole, which did not give a precipitate after treatment with sodium alcoholate according to Claisen [5]. This fact indicated that the isoxazole prepared by us is indeed the 3-substituted isomer.



In order to solve more definitely the question of the degree of purity of the 3-substituted isomers prepared by us in the cases of 3-α'-chloroethylisoxazole and the previously described 3-chloromethylisoxazole, we accomplished the reduction of these α'-chloroalkylisoxazoles into the corresponding alkylisoxazoles and studied the compounds obtained thusly from the point of view of possible presence in them of admixtures of the 5-substituted isomers. The α'-chloroalkylisoxazoles are reduced smoothly to the corresponding alkylisoxazoles by means of zinc dust in acetic acid or alcohol.



The cleavage of the resulting methyl- and ethylisoxazoles by sodium alcoholate according to Claisen [5] showed that methylisoxazole contained 10% and ethylisoxazole contained 3% of the 5-substituted isomer. Since the absence of isomerization of the 3-substituted isomer under the conditions of reduction was confirmed by a special experiment, the above result makes us admit that the reaction of chloromethyl β-chlorovinyl ketone with hydroxylamine does not proceed completely in a single path, as it had been indicated by us previously [1, 6]. At the same time this shows that the predominant direction of the reaction of α'-chloroalkyl β-chlorovinyl ketones with hydroxylamine is still the formation of the 3-substituted isoxazole, which fact confirms the thought, expressed in the first part of this paper, about the material effect of the chlorine atom in α'-position in the alkyl residue in β-chlorovinyl ketones on the direction of reaction with hydroxylamine.

In conclusion it should be mentioned that despite the lack of specificity in the course of the reaction of α'-chloroalkyl β-chlorovinyl ketones with hydroxylamines, this reaction is still at the present time the best method for a directed synthesis of 3-substituted isoxazoles insofar as all the existing methods of synthesis always yield a mixture of 3- and 5-substituted isomers. The method of reduction of α'-chloroalkylisoxazoles, developed by us, makes accessible the pure 3-alkylisoxazoles.

## EXPERIMENTAL

α-Chloropropionyl chloride was prepared by chlorination of propionyl chloride with sulfuryl chloride by the Kharash method [7], with modifications which had been described by us previously [8]. The yield was 60%; b.p. 109-111°.

α'-Chloroethyl β-chlorovinyl ketone. Into a three-necked flask provided with a stirrer, a reflux condenser, a gas inlet tube and a thermometer, there was placed a solution of 28.6 g of α-chloropropionyl chloride in 80 ml of carbon tetrachloride. A not too energetic stream of acetylene was passed through the solution while over one hour at 15-20°, with stirring, there was added 29.5 g of anhydrous aluminum chloride in small portions. The acetylene was introduced at this temperature for four hours longer. Then the reaction mixture was poured on ice, the layer of carbon tetrachloride was separated, the aqueous layer was extracted with ether and the combined extracts and the main portion of the product were dried over magnesium sulfate. The α'-chloroethyl β-chlorovinyl ketone was isolated by distillation. The yield was 19.5 g (55%); b.p. 69-70° at 11 mm.

$n^{20}D$ 1.4960, $d^{20}_4$ 1.2640, $MR_D$ 35.36; calculated 34.57; $EMR_D$ 0.79.
Found %: C 39.49, 39.19; H 4.18, 4.31. $C_5H_6OCl_2$. Calculated %: C 39.25; H 3.95.

The ketone was a colorless oily liquid with a characteristically sharp odor; it was a strong lachrymator. It darkens rapidly in storage, but can be preserved for a long time in the cold in ether solution.

3-α'-Chloroethylisoxazole. To the solution of 12.7 g of hydroxylamine hydrochloride in 70 ml of methanol there was added 20.0 g of α'-chloroethyl β-chlorovinyl ketone. After six hours of refluxing the mixture was poured into 250 ml of water and extracted several times with ether; the extracts were dried over magnesium sulfate, the solvent was distilled and the residue was distilled, collecting the fraction with b.p. 69-70° at 20 mm. The yield was 14.6 g (86%).

$n^{20}D$ 1.4729, $d^{20}_4$ 1.1869, $MR_D$ 30.28; calculated 30.87.*
Found %: N 10.62, 10.53. $C_5H_6ONCl$. Calculated %: N 10.64.

The substance is a colorless oil with a characteristic odor. It is a weak lachrymator.

Reduction of 3-chloromethylisoxazole. 1. To the solution of 36.5 g of 3-chloromethylisoxazole in 200 ml of 90% alcohol there was added with stirring 100 g of zinc dust. After refluxing for 1.5 hours, the precipitate was filtered off, washed on the filter with 50 ml of alcohol and to the hot mother liquor there was added a hot saturated solution of 100 g of cadmium chloride in water. The precipitate of the cadmium complex of methylisoxazole, which formed after one day, was filtered off and washed on the filter with 50 ml of cold saturated solution of cadmium chloride. The methylisoxazole was isolated by decomposing the cadmium complex as described earlier [1]. There was obtained 15.3 g of the product (58%) with b.p. 117.5-119° at 750 mm.

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*The increment of nitrogen in the ring was taken as 2.84 in the paper [1].

$n^{20}D$ 1.4345, $d^{20}_4$ 1.0189, $MR_D$ 21.27; calculated 21.39.

According to literature data for 3-methylisoxazole [5]: b.p. 118.5°, $n^{20}He$ 1.4345, $d^{20}_4$ 1.022; according to data [1]: b.p. 118°, $n^{20}D$ 1.4345, $d^{20}_4$ 1.0206; for 5-methylisoxazole according to data [3]: b.p. 121-122°, $n^{20}D$ 1.4368, $d^{20}_4$ 1.0224.

The determination of the content of the α-isomer in the methylisoxazole was performed as described previously [1]. After treatment of 2.97 g of methylisoxazole with sodium ethoxide (from 1.0 g of sodium) in 90 ml of anhydrous ethanol, there was obtained 0.410 g of sodiocyanoacetone, which corresponded to the content of 11% of 5-methylisoxazole. Phenylhydrazone of cyanoacetone has m.p. 100-101° (from alcohol).

According to data [9], m.p. 101-102°; according to data [1], m.p. 100°.

2. To the solution of 23.5 g of 3-chloromethylisoxazole in 100 ml of glacial acetic acid there was added with stirring 30.0 g of zinc dust, the temperature being maintained at not above 70°. After termination of the self-heating of the reaction mixture (3 hours), the mixture was heated on a boiling water bath for one hour. Then the precipitate was filtered off, washed on the filter with 20 ml of glacial acetic acid and the mother liquor was diluted with 300 ml of water, carefully neutralized with sodium carbonate and extracted several times with ether. The ethereal extracts were dried over magnesium sulfate, the ether was distilled from a flask with a 75 cm fractionating column, and the residue was distilled, collecting the fraction with b.p. 118-122° at 750 mm. The yield was 9.7 g (59%).

$n^{20}D$ 1.4360, $d^{20}_4$ 1.0202, $MR_D$ 21.23; calculated 21.39.

By the action of sodium ethoxide there was obtained from 2.235 g of methylisoxazole, by the above method, 0.285 g of sodiocyanoacetone (indicative of 10% of 5-methylisoxazole); phenylhydrazone of cyanoacetone had m.p. 99° (from alcohol).

Reduction of 3-α'-chloroethylisoxazole was run in glacial acetic acid analogously to the one described above. From 7.0 g of chloroethylisoxazole and 5.4 g of zinc dust in 25 ml of glacial acetic acid there was obtained 2.5 g (54%) of ethylisoxazole.

B.p. 137-139° at 740 mm, $n^{20}D$ 1.4370, $d^{20}_4$ 0.9874, $MR_D$ 25.80; calculated 26.00.

For a mixture of 5-ethylisoxazoles, according to [1]: b.p. 139-140°, $n^{20}D$ 1.4440, $d^{20}_4$ 0.9916.

From 1.015 g of ethylisoxazole and sodium ethoxide there was obtained 0.037 g (3% of 5-α'-ethylisoxazole) of sodio-1-cyano-2-butanone. Phenylhydrazone of 1-cyano-2-butanone had m.p. 87-88° (from alcohol). For phenylhydrazone of 1-cyanobutanone according to [1]: m.p. 88-89°.

## SUMMARY

1. It was shown that α'-chloroalkyl β-chlorovinyl ketones react with hydroxylamine with formation of 3-α'-chloroalkylisoxazoles with a small admixture of 5-substituted isomers.

2. A method of preparation of 3-alkylisoxazoles was developed by the reduction of the corresponding 3-α'-chloroalkylisoxazoles with zinc dust.

## LITERATURE CITED

[1] N. K. Kochetkov, A. N. Nesmeianov and N. A. Semenov, Bull. Acad. Sci. USSR, ser. chem. 1952, 87.*

[2] N. K. Kochetkov, E. D. Khomutova, M. Ia. Karpeiskii and A. Ia. Khorlin, J. Gen. Chem. 27, 452 (1957).*

[3] N. K. Kochetkov, Bull. Acad. Sci. USSR, ser. chem. 1954, 47.*

[4] A. N. Nesmeianov, N. K. Kochetkov and M. I. Rybinskaia, Bull. Acad. Sci. USSR, ser. chem. 1950, 350.

[5] L. Claisen, Ber. 36, 3673 (1903).

---

*Original Russian pagination. See C. B. Translation.

[6] N. K. Kochetkov and A. Ia. Khorlin, J. Gen. Chem. 25, 1212 (1955).*

[7] M. Kharash and N. Brown, J. Am. Chem. Soc. 62, 925 (1940).

[8] N. K. Kochetkov, A. Ia. Khorlin, B. P. Gottikh and A. N. Nesmelanov, Bull. Acad. Sci. USSR, ser. chem. 1956, 1053.*

[9] L. Claisen, Ber. 42, 59 (1909).

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* Original Russian pagination. See C. B. Translation.

# A STUDY IN THE FIELD OF THIOSULFONIC ACIDS

## IV. CONCERNING THE MECHANISM OF THE REACTION OF FORMATION OF THIOSULFONATES

B. G. Boldyrev and T. A. Trofimova

Alkane- and arenethiosulfonic acids may be prepared in the form of salts $RSO_2SM$ (I) by the action of halides of sulfonic acids on aqueous solutions of potassium hydrosulfide [1-4].

Owing to the fact that in the process of the reaction there occurs a separation of elemental sulfur, which on further heating of the reaction mixture goes into solution, it is supposed [2, 3] that the formation of thiosulfonates (I) proceeds according to the following general scheme of reactions:

$$RSO_2Cl + K_2S \longrightarrow RSO_2K + KCl + S, \tag{1}$$

$$RSO_2K + S \longrightarrow RSO_2SK. \tag{2}$$

Specifically in this manner did Blomstrand [1] prepare and isolate for the first time the potassium salt of p-toluenethiosulfonic acid, without discussing the mechanism of the reaction itself at that time.

Later, Spring [2] repeated Blomstrand's experiments with the example of preparation of benzenethiosulfonate and expressed the supposition that the reaction proceeds through a stage of formation of a salt of sulfinic acid. He also reported that he was able to prepare the same product by the reaction of a salt of benzenesulfinic acid with sulfur and to isolate from the reaction mixture a salt of sulfinic acid. The author, however, did not cite the technique of the experiments nor did he give the proofs of identity of the products obtained by the various routes.

For this reason we considered it interesting to check in this work the correctness of the previously suggested concepts about the mechanism of the reaction of formation of thiosulfonates, especially since this method specifically – reaction of sulfonyl chlorides with potassium hydrosulfide – had been used previously [5-9] for the preparation and isolation of over twenty salts of various thiosulfonic acids.

The possibility of formation of thiosulfonates according to reaction (2) was decided to be tested by us with the example of preparation of the potassium salt of acetylthiosulfanilic acid (II). For this purpose p-acetylaminobenzenesulfonyl chloride was converted, by the reaction with an aqueous solution of potassium hydrosulfide, into thiosulfonate (II). By the usual method [10] from the same chloride there was prepared the p-acetylaminobenzenesulfinic acid; by heating the alkaline solution of its potassium salt with elemental sulfur we obtained product (V), the identification of which was made by the scheme shown below.*

The products of the reactions (II) and (V) isolated by us turned out to be completely identical with each other: they were colorless crystalline substances with m.p. 256°; no depression was found in their mixed melting point.

Completely identical also were their derivatives – allyl esters (III) and (VI), as well as the products of deacetylation – potassium salts of [(IV) and (VII)] thiosulfanilic acid.

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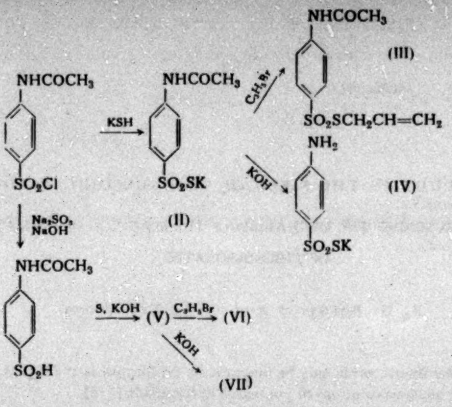
* Substances (II-IV) were first prepared by M. A. Belous [11].



Thus, the supposition expressed previously by other authors that the salts of thiosulfonic acids may be synthesized by the reaction of salts of sulfinic acids with elemental sulfur [2], was completely confirmed.

This fact, however, does not speak as yet about the fact that the preparation of thiosulfonates (I) from chlorides of sulfonic acids and hydrosulfides of alkali metals proceeds through the stage of formation of salts of sulfinic acids.

In order to confirm the mechanism of this reaction one should isolate potassium sulfinate directly from the reaction mixture after the preparation of the thiosulfonate (II) before the solution of the elemental sulfur which formed during the reaction.

Our first attempts to isolate the sulfinate from such a reaction mixture ended in failure since even at low temperature the potassium sulfinate reacted readily with elemental sulfur with formation of the thiosulfonate, which fact hindered the isolation of small amounts of the salt of the sulfinic acid remaining in the solution.

However, by running the reaction with a dilute solution of potassium hydrosulfide at −2° it turned out to be possible to retard to a considerable degree the secondary reaction of formation of the thiosulfonate and to isolate from the reaction mixture some p-acetylaminobenzenesulfinic acid which was then identified by its conversion to the thiosulfonate (II) and then into the allyl ester (III) of acetylthiosulfanilic acid.

This confirmed that the preparation of thiosulfonates (II) by the reaction of halides of sulfonic acids with hydrosulfides of alkali metals actually does proceed through the intermediate stage of formation of salts of sulfinic acids.

## EXPERIMENTAL

The starting materials for the syntheses of thiosulfonate (II) – chloride of acetylsulfanilic acid and p-acetylaminobenzenesulfinic acid – were prepared by us through the usual paths [12, 10].

Preparation of potassium acetylthiosulfanilate. a) From the chloride of acetylsulfanilic acid and potassium hydrosulfide. This synthesis was run by us under conditions described previously [7, 8] for other thiosulfonates. Here from 280 g of the chloride of acetylsulfanilic acid and potassium hydrosulfide prepared by saturation with hydrogen sulfide of a solution of 150 g of potassium hydroxide in 300 ml of water, there was prepared 215 g (70%) of colorless crystalline substance with m.p. 256°. The product was readily soluble in water and boiling alcohol; it was insoluble in benzene, ether, acetone and chloroform; it crystallized from alcohol in the form of reactangular plates.

Found %: S 23.70, 23.67. $C_8H_8O_3NS_2K$. Calculated %: S 23.81.

b) From potassium p-acetylaminobenzenesulfinate and elemental sulfur. p-Acetylaminobenzenesulfinic acid (26.5 g) was dissolved in an excess[*] of 30% solution of potassium hydroxide (10.2 g in 26 ml of water) and heated with 4.3 g of thoroughly powdered elemental sulfur on a boiling water bath for 2.5 hours. After the heating the sulfur was almost completely dissolved and the solution had a reddish-orange color, characteristic of polysulfides. After addition of charcoal and filtration, the solution was evaporated to dryness on a water bath and the dry residue was extracted with alcohol and the resulting crystalline product was recrystallized from the same solvent.

The yield of colorless thiosulfonate with m.p. 256° was 22.2 g (63.2%).

Found %: S 23.52, 23.48. $C_8H_8O_3NS_2K$. Calculated %: S 23.81.

The mixed melting point of this product with the acetylthiosulfanilate prepared by Method a showed no depression.

Preparation of allyl ester of acetylthiosulfanilic acid. The allyl ester (III) was synthesized by us by the reaction of potassium acetylthiosulfanilate with allyl bromide in aqueous acetone solution by the method described for the preparation of analogous esters of other thiosulfonic acids [4]. Here from 15.0 g of potassium salt and 6.8 g of allyl bromide there was obtained 9.9 g (66.6%) of allyl ester (III).

After recrystallization from 40% alcohol the product appeared as a colorless crystalline substance with m.p. 59-60°. It was poorly soluble in water, excellently soluble in alcohol, ether, acetone and other organic solvents; it crystallized from 40% alcohol in the form of crystals having the shape of triangular prisms.

Found %: S 23.55. $C_{11}H_{13}O_3NS_2$. Calculated %: S 23.63.

The same ester was prepared by an analogous route from product (V); the mixed melting point of the esters showed no depression.

Preparation of potassium thiosulfanilate. Potassium acetylthiosulfanilate (76.5 g) was introduced into 170 ml of 10% solution of potassium hydroxide and was heated for two hours on a boiling water bath with mechanical stirring. Then to the resulting orange solution under the same conditions there was added dropwise 10% acetic acid until the mixture became neutral to phenolphthalein. After addition of some activated charcoal and a ten-minute standing, the solution was filtered and from the filtrate on cooling there precipitated the colorless crystals of potassium thiosulfanilate. The product was filtered off and washed with alcohol, and the filtrate was concentrated to half the original volume after which from it precipitated an additional considerable amount of the same product. After two recrystallizations from alcohol there was obtained the colorless crystalline substance with m.p. 237-238° (with decomposition). The yield of the salt was 41.0 g (63.7%).

Potassium thiosulfanilate was readily soluble in water and boiling alcohol; it was insoluble in ether, benzene, chloroform and acetone; it crystallized from alcohol in the form of thin needles.

Found %: S 28.11. $C_6H_6O_2NS_2K$. Calculated %: S 28.21.

The deacetylation of product (V) was run in analogous manner. The mixed melting point of the thiosulfonates showed no depression.

Isolation of p-acetylaminobenzenesulfinic acid from the reaction mixture in the preparation of acetylthiosulfanilate. The solution of 30 g of potassium hydroxide in 60 ml of water was saturated with hydrogen sulfide and diluted with 4 parts of water; then at the temperature of −2° with mechanical stirring there was added to it 60 g of previously recrystallized chloride of acetylsulfanilic acid. The resulting precipitate of sulfur was filtered off and to the dark green solution there was added concentrated sulfuric acid until the filtrate became colorless. Then the filtrate was chilled with a mixture of ice and salt and to it there was added an excess of acid until a colorless crystalline precipitate formed. After recrystallization from water there was obtained 9.52 g (19.2%) of product with m.p. 151-153°.

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[*] In case of equimolar amount of alkali the reaction between the sulfinate and the sulfur proceeds extremely slowly; it is possible that the formation of potassium polysulfides aids the more energetic course of the main reaction of formation of the salt of thiosulfonic acid. In the preparation of benzenethiosulfonate by the same method the reaction proceeds smoothly and without excess of alkali even in the case in which one uses a previously prepared salt of benzenesulfinic acid; it is true that in this case the medium shows an alkaline reaction and hence it is possible to admit the formation of small amounts of polysulfides.

Found %: S 16.29, 16.11. $C_8H_9O_3NS$. Calculated %: S 16.10.

The mixed melting point of the isolated product with the sulfinic acid prepared by the usual route showed no depression.

The identification of p-acetylaminobenzenesulfinic acid was made by its transformation into the thiosulfonate by heating with sulfur in an alkaline solution and then by conversion of this to allyl ester of acetylthiosulfanilic acid.

## SUMMARY

1. By an example taken from synthesis of potassium acetylthiosulfanilate there was confirmed the mechanism of the reaction of preparation of salts of thiosulfonic acids from halides of sulfonic acids and hydrosulfides of alkali metals through the intermediate stage of formation of salts of sulfinic acids.

2. It was shown that it is possible to synthesize the thiosulfonates from salts of sulfinic acids and elemental sulfur.

## LITERATURE CITED

[1] C. W. Blomstrand, Ber. 3, 957 (1870).

[2] W. Spring, Ber. 7, 1157 (1874).

[3] R. Otto, Ber. 15, 127 (1882).

[4] M. A. Belous and I. Ia. Postovskii, J. Gen. Chem. 20, 1701 (1950).*

[5] B. G. Boldyrev and A. T. Zakharchuk, Doklady Akad. Nauk SSSR 94, 877 (1954).

[6] B. G. Boldyrev and A. K. Litkovets, Doklady Akad. Nauk SSSR 107, 697 (1956).*

[7] B. G. Boldyrev and A. K. Litkovets and T. A. Trofimova, J. Gen. Chem. 26, 3360 (1956).*

[8] B. G. Boldyrev and T. A. Trofimova, J. Gen. Chem. 27, 1006 (1957).*

[9] B. G. Boldyrev, Sci. Notes of L'vov Polytechnic Institute, ser. chem. technol. No. 2, 71 (1956).

[10] Syntheses of organic preparations, vol. 1, 68 (1949).**

[11] M. A. Belous, Dissertation "Syntheses and structure of new antibacterial substances in the sulfone series," Sverdlovsk (1947).**

[12] A. M. Berkengeim, Manual of synthetic medicinal and odoriferous substances and photographic reagents, Moscow-Leningrad, State Technical Press, p. 133 (1942).**

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*Original Russian pagination. See C. B. Translation.

**In Russian.

# A STUDY OF THE MECHANISM OF DIAZOEXCHANGE* IN AZO DYES OF THE NAPHTHALENE SERIES MADE BY MEANS OF THE HEAVY NITROGEN ISOTOPE

B. A. Geller

A transfer of a diazo group is a phenomenon which is rather often met in the chemistry of dyes. To this group of reactions belong, for example, the transformation of the mixture of p-sulfobenzenediazonium chloride with p-toluidine into sulfanilic acid and p-toluenediazonium chloride, discovered by Gries [1], the preparation of mixed aminoazo compounds from primary aromatic amines and diazo compounds in weakly acid media [2] and others. Saunders connects these phenomena with the existence in the solution of an equilibrium between the diazo compound, the salt of the amine and nitrous acid formed in hydrolysis.

Replacement of diazo compounds by other diazo compounds was found also in the series of stable azo compounds. Thus, L'vov [3], evidently was the first to discover that in the action of p-nitro- or o-chloro-p-nitrobenzenediazonium compounds on p-sulfobenzeneazo-β-naphthol in an alkaline medium there are formed respectively p-nitro- or o-chloro-p-nitrobenzeneazo-β-naphthols. Analogous reactions were studied more extensively by Filippychev and Chekalin [4]. According to their data, the diazo compounds containing the more negative substituents and behaving more actively in the usual azo coupling, displace the less active diazo compounds from dyes. In the series of substances studied by these authors the following disposition was found in order of activity of the diazo compounds: p-nitroaniline > benzidine > dianisidine > sulfanilic acid > amino-C-acid > α-naphthylamine > m-xylidine > aniline > p-aminosalicylic acid, in which series each compound displaces the following ones from dyes. It was also established that the diazo exchange does not occur with azo components from the benzene series. Using the analogy with other reactions in the naphthalene series [6, 9], the authors suggest that diazoexchange should proceed through the formation of an unstable intermediate with quinoid structure.

In this work there was studied, for the clarification of the mechanism of diazoexchange and specifically the location of the bond rupture, the reaction of 4-sulfobenzene-1-azo-2-naphthol (acid orange) (I) with p-nitrobenzenediazonium hydroxide (II)** using the heavy nitrogen isotope. In one series of experiments the reaction was run with (II) prepared from p-nitroaniline and labeled sodium nitrite with 9.0% of $N^{15}$. In this case the labeled nitrogen atoms are shown in reaction scheme (1) below by the symbol $N^{15}$. The other nitrogen atoms must be regarded as unenriched ones (i.e., with 0.37% of $N^{15}$) regardless of the symbols used. In another series of experiments the heavy nitrogen was introduced into (I) by coupling sulfanilic acid diazotized with $NaN^{15}O_2$ with β-naphthol. In this case the nitrogen atoms with 9% of $N^{15}$ and shown as N* while the other nitrogen atoms (regardless of symbols) are plain atoms with 0.37% of $N^{15}$. The study was made by the scheme:

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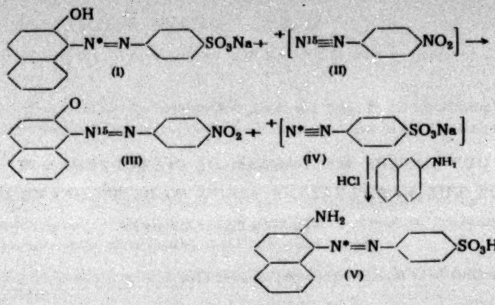
*The term "diazoexchange" used not too satisfactorily at times in the transfer of one diazo group in coupling reactions of diazo compounds with primary aromatic amines in weakly acid media, reflects well the nature of reactions similar to that studied in this work. Since diazo groups cannot move of themselves, it is clear that the term diazoexchange means an exchange in which diazo compounds participate (diazo components).

**The hydrochloride of (II), used for the reaction, is transformed into the diazonium hydroxide under the conditions of alkaline medium which results from mixing of the solutions.

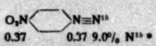
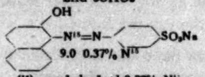


(1)

After the diazoexchange, the separated p-sulfobenzenediazonium compound (IV) was coupled with β-naphthylamine. The dyes (III) (para red) and (V) were purified, the nitrogen contained in them was converted to ammonium chloride and this was subjected to isotope analysis. The results of the analyses are given in Table 1. The analysis of the dyes in the first series of experiments showed that practically all the excess of $N^{15}$ (over the natural content of 0.37% of $N^{15}$) is located in (III). The results of the second series of experiments showed that the $N^{*}$-atom in (I) does not enter the dye (III), i.e., that the link of this nitrogen atom to the naphthalene nucleus is ruptured.

Therefore, the diazo components preserve during the transfer the nitrogen atoms belonging to them. The distribution of $N^{15}$ which corresponds to this is shown in scheme (1). This result agrees with the mechanism of an electrophilic displacement, commonly accepted at present for the reaction of azo coupling. Evidently, the diazoexchange should be regarded as an example of azo coupling in which the site of attack by the diazonium ion occupied not by hydrogen but by some other substitutent. Many cases are described in the literature for diazo coupling with a simultaneous displacement of $SO_3H$, COOH, Br, I, CHO, and other groups [5-8]. In the present case the displaced substituent is another diazo compound. The analogy with azo coupling may be seen also in the coincidence of the series of diazo compounds which displace each other, shown above, with the series made in order of their activities. Thus the reaction of the diazoexchange should proceed through an intermediate complex of quinoid type [5, 10, 11] which may be represented by scheme (2).

TABLE 1

<table>
<tr><th rowspan="4">Reaction products</th><th colspan="6">Starting substances</th></tr>
<tr><th colspan="3">1st series<br><br>(I) – unlabeled 0.37% $N^{15}$</th><th colspan="3">2nd series<br><br>(II) – unlabeled 0.37% $N^{15}$</th></tr>
<tr><th colspan="6">$N^{15}$ (in atom %)</th></tr>
<tr><th>found</th><th>Calculated for: scheme (2)</th><th>Calculated for: scheme (3)</th><th>found</th><th>Calculated for: scheme (2)</th><th>Calculated for: scheme (3)</th></tr>
<tr><td>Dye (III)</td><td>3.1<br>2.8</td><td>3.25</td><td>0.37</td><td>0.42<br>0.51</td><td>0.37</td><td>3.25</td></tr>
<tr><td>Dye (V)</td><td>0.63<br>0.71</td><td>0.37</td><td>3.25</td><td>—</td><td></td><td></td></tr>
</table>

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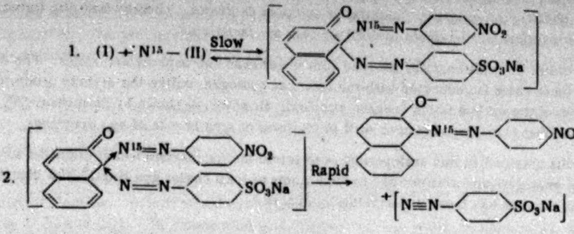
* Numbers under nitrogen atoms indicate the content of $N^{15}$ in them.

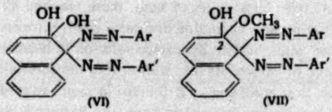


(2)

Since the hydroxy compounds of naphthalene participate in the azo coupling reaction in the form of naphtholate ions, in scheme (2) we mean the ion $-OC_{10}H_6N_2C_6H_4SO_3Na$ to be the substance (I).

Our results, obtained with $N^{15}$, do not permit us to make a selection between mechanisms $S_E2$ and $S_E3$. However, as it was shown by the study of the kinetic isotope effect of hydrogen [10], azo coupling in all cases proceeds in two stages by $S_E2$ mechanism. There is no basis to consider that the diazoexchange proceeds differently from azo coupling in which the formation of the intermediate complex is complicated by steric hindrance. Therefore one may assume that diazoexchange also process by the $S_E2$ mechanism.

The intermediate complex of quinoid type (VI), proposed by Filippychev and Chekalin [4], cannot form in diazoexchange in hydroxy azo dyes, since hydroxy compounds enter this reaction, as well as that of diazo coupling, in the form of phenolate (or naphtholate) ions. Therefore there is no basis to bring OH groups at this point of discussion. The electron density at the ion $-\underset{\curvearrowright}{\mathrm{O}}-\mathrm{C}\begin{smallmatrix}/\!/\\ \backslash\end{smallmatrix}$ is sufficient to compensate for the positive charge of carbon. It is possible, however, that in the diazoexchange of ethers of naphthols, in which the alkyl groups are not cleaved, there occurs the formation of an intermediate complex (VII) since in this case the electrons of oxygen of the methoxy group cannot completely compensate for the positive charge on carbon $C_2$ caused by the attack of the electrophilic reagent.



(VI) (VII)

(3)

Diazoexchange may differ in the details of the mechanism of electrophilic displacement from the usual azo coupling in which a displacement of a proton occurs. The cleavage of the proton from the transitional complex may be aided by the acceptors $HO^-$, $H_2O$ and others, which are present in the reaction medium, since hydrogen by the steric conditions is readily available to the ions or molecules surrounding it and, in addition, is susceptible to formation of hydrogen bonds. Conversely, nitrogen in a complex molecule of the azo compound does not possess such properties and therefore it must be supposed that the donor-acceptor mechanism plays but a small role in the cleavage of the diazonium cation in the diazoexchange.

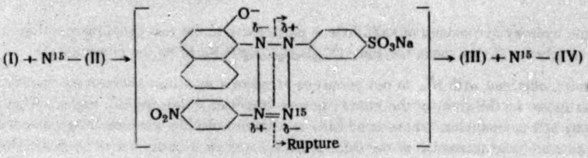
It is also impossible to accept that the displacement of diazo compounds is determined by the relative stabilities of the reacting diazonium cations, since it is specifically the more stable cation that enters the compound while the less stable one is liberated and passes into solution.

It is most probable that the decomposition of the transitional complex is aided by an electron shift in the system of the joined diazo compounds [as shown in scheme (2)] directed toward the more electrophilic diazo compound.

The reaction of diazoexchange, as indicated above, does not occur in dyes with azo components of the benzene series. This may be explained only by the lesser tendency of the benzene derivatives to form quinoidal structures. The ability of various systems to form quinones is characterized by their oxidation potential. With introduction of electron-donor substituents (in case of naphthalene – a second benzene ring) which increases the total electron density, the oxidation potential of quinones decreases. Thereby both the formation of quinones and the progress of reactions of electrophilic displacement are facilitated.

The reactions of usual coupling proceed both in benzene and naphthalene series. The absence of a sharp distinction in these cases is connected with the fact that hydrogen, unlike the arylazo group, does not lower the negative charge of the carbon which is being attacked. However, as shown by Burmistrov [5], the smaller oxidation potential of quinones is displayed here as well in the form of greater rate of azo coupling.

The results obtained in this work permit us to refuse the mechanism which might be suggested on the basis of a number of analogies and abilities of nitrogen atoms to form chains and rings.* The distribution of $N^{15}$ in this case is opposite to what was found experimentally (Table 1).



(3)

## EXPERIMENTAL

Sodium nitrite $NaN^{15}O_2$ was prepared from ammonia with 9.0% of $N^{15}$ by the scheme:

$$N^{15}H_3 \xrightarrow[\text{Pt, }600^\circ]{O_2} N^{15}O_2 \xrightarrow{Ba(OH)_2} Ba(N^{15}O_3)_2 + Ba(N^{15}O_2)_2 \xrightarrow{H_2O_2}$$

$$\longrightarrow Ba(N^{15}O_3)_2 \xrightarrow{Na_2SO_4} NaN^{15}O_3 \xrightarrow[350^\circ]{Pb} NaN^{15}O_2$$

Oxidation of ammonia with air over platinum catalyst was run in a flow system at 600°, the velocity of the gas stream being 10 liters per hour with the content of ammonia being 8% or lower. Evidently, owing to the unstable conditions, it was impossible to attain high yields of $NO_2$: these reached 60-65%. The nitrogen oxides were absorbed by a saturated solution of barium hydroxide and were finally frozen out with liquid air. Solid nitrogen dioxide was then treated with the same barium hydroxide solution in hermetically tight apparatus. Excess barium hydroxide was removed by passage of carbon dioxide stream into the solution. The barium carbonate was filtered off after boiling and the solution, now acidified by 2-3 drops of concentrated nitric acid, was oxidized with hydrogen peroxide with heating to 70°. The solution was neutralized with barium hydroxide (its excess was again removed with carbon dioxide) and was evaporated to dryness after filtration. The resulting $Ba(N^{15}O_3)_2$ was transformed into $NaN^{15}O_3$ by treatment with an equivalent amount of sodium sulfate in a hot solution.

By heating $NaN^{15}O_3$ with lead powder to 350°, the former was changed into $NaN^{15}O_2$ [14, 15].

$N^{15}$-Acid orange (I) labeled with heavy nitrogen was prepared by diazotization of sulfanilic acid with sodium nitrite containing 9.0% of $N^{15}$ with subsequent coupling with β-naphthol. The dye was recrystallized three times from water for removal of sodium chloride.

Diazoexchange between Acid orange and p-nitrobenzenediazonium compound. The conditions for the diazoexchange were so selected as to secure a good yield of (III) at the same time producing the optimum conditions for coupling of (IV) with β-naphthylamine. One g (0.0028 mole) of (I) was dissolved in water with 0.8 g of sodium carbonate and was then mixed with p-nitrobenzenediazonium chloride, prepared from 0.26 g of p-nitroaniline (0.0019 mole) with 0.9 ml of concentrated hydrochloric acid, at 0°. The medium remains alkaline during this operation. After 30 minutes standing in ice the precipitate of (III) and (I) was filtered off as rapidly as possible. The filtrate was acidified with 7 ml of concentrated hydrochloric acid and mixed with the hydrochloric acid solution of 0.27 g of β-naphthylamine. The precipitated dyes were filtered off after several hours, washed with water and dried. The p-nitrobenzeneazo-β-naphthylamine was extracted with hot benzene and the residual (V) was recrystallized from alcohol (3 : 1).

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*Formation of intermediate cyclopentazanes was proposed for the reaction of diazo compounds with hydrazoic acid and has been confirmed by isotope studies [12]. Formation of mixed four-membered rings from nitrogen and carbon atoms may occur in the presence of azo- or methylenimino group [13]; here the cyclodimers decompose instantly at times, while at times they are obtained in the form of stable compounds.

The precipitate of (III) and (I) was washed on the filter with hot water until the filtrate became only slightly pigmented. The (III) which remained on the filter was dried and repeatedly recrystallized from glacial acetic acid. The yields of crude dyes were 50-60% of theoretical.

Qualitative analysis (fusion with metallic sodium) failed to show any sulfur in (III); the tests of an aqueous extract with p-aminodiethylaniline, sodium nitroprusside and lead acetate were all negative. This shows the absence of admixtures of (I) and (III). In connection with this fact we are unable to explain the deviations in the content of $N^{15}$ in (III) from values computed by scheme (2). The cause for this may lie in the parallel progress of the process by mechanism (3); however the degree of its participation may make up 2-5% which lies close to the experimental error.

TABLE 2

| Number of recrystallizations | % $N^{15}$ in (III) |
|---|---|
| 2 | 0.59 |
| 3 | 0.44 |
| 4 | 0.52 |
| 5 | 0.47 |
| 6 | 0.53 |
| Average | 0.51 |

The control of purity of dye (III) in one experiment was also made by the determination of the isotopic composition of nitrogen after each crystallization. As it is evident from Table 2, the isotopic composition is practically unchanged after the third recrystallization.

The small variations may be explained by the difficulty of the treatment of $N=N$ and $NO_2$ groups by the Kjeldahl method: there occurs the elimination of heavy or light nitrogen, respectively, in insignificant volumes which cannot be subjected to any computation.

The dyes were qualitatively identified by their physical properties (color, solubility) with those prepared synthetically from individual substances. In addition, the melting point of (III) was determined; this agreed with the literature data.

## Isotopic Nitrogen Analysis

A portion of the dyes was treated by the Kjeldahl method altered for nitro and azo compounds [16]. The method was checked with dye (III) that was synthesized by us and gave satisfactory results. The ammonia was distilled from reaction mixture into hydrochloric acid. The resulting ammonium chloride was precipitated with sodium cobaltinitrite * from aqueous alcoholic solution (1 : 1) and was again converted to ammonia by decomposition of the precipitate with alkali.

The isotopic analysis of nitrogen samples, obtained from the ammonium chloride by hypobromite oxidation, was run in a mass spectrometer by the measurement of 28 and 29 peaks. The relative errors of the determination were not over 2-3%. The results are shown in Table 1.

I thank A. I. Brodskii for his aid in this work.

## SUMMARY

The diazoexchange in azo dyes of the naphthalene series was studied on the example of reaction between p-sulfobenzeneazo-β-naphthol and p-nitrobenzenediazonium hydroxide. The results, obtained with the aid of labeled nitrogen, agree with the mechanism of an electrophilic displacement. Suppositions were made about the details of the mechanism of the reaction of diazoexchange.

## LITERATURE CITED

[1] P. Gries, Ber. 15, 2184 (1882).

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* The reagent for precipitation was prepared by solution of 11.25 g of $Na_3Co(NO_2)_6 \cdot 0.5\ H_2O$ and 12.50 g of $NaNO_2$ in 100 ml of water. The solution was filtered after one day.

[2] K. H. Saunders. The aromatic diazo compounds and their technical applications (1949).

[3] A. Lwoff, Ber. 41, 1096 (1908).

[4] S. F. Filippychev and M. A. Chekalin, Analine Dye Industry 5, 76 (1935).

[5] S. I. Burmistrov, J. Gen. Chem. 20, 277 (1950).*

[6] N. N Vorozhtsov, Bases for synthesis of intermediate products and dyes, (1955).**

[7] I. M. Kogan, Chemistry of dyes (1956).**

[8] S. F. Filippychev, Chemistry and technology of azo dyes, vol. 1 (1938).**

[9] K. H. Meyer, A. Irschik and H. Schlosser, Ber. 47, 1741 (1914); Ber. 52, 1468 (1919).

[10] H. Zollinger, Helv. Chim. Acta 38, 1597, 1617 (1955).

[11] C. K. Ingold, Structure and Mechanism in Organic Chemistry (1953).

[12] K. Clusius and M. Vecchi, Helv. Chim. Acta. 39, 1469 (1956).

[13] I. L. Knuniants, V. L. Diatkin and N. P. Gamborian, Progr. Chem. 25, 784 (1956).

[14] A. A. Bothner-By and L. Friedman, J. Am. Chem. Soc. 73, 5391 (1951).

[15] V. I. Maimind et al., J. Gen. Chem. 26, 1962 (1956).*

[16] A. P. Groshev, Technical analysis (1953).**

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** In Russian.

# REACTION OF N,N-DICHLOROBENZENE SULFONAMIDE WITH POLYHALOGEN DERIVATIVES OF METHANE. I.

A. E. Kretov and M. M. Kremlev

An evolution of chlorine and formation of benzenesulfonyl chloride was observed by us on heating N,N-dichlorobenzenesulfonamide (Dichloramide B) with carbon tetrachloride in the presence of anhydrous aluminum chloride. The chlorine evolution was so abundant that it demanded the supposition that carbon tetrachloride took part in the reaction (the carbon tetrachloride was used in a large excess).

Experiments with various amounts of the dichloramine and aluminum chloride gave the following results (Table 1).

TABLE 1

| Taken for the reaction (in moles) | | | Obtained (in moles) | |
|---|---|---|---|---|
| Dichloramine B | $AlCl_3$ | $CCl_4$ | $Cl_2$ | $C_6H_5SO_2Cl$ |
| 0.1 | 0.1 | 1.55 | 0.202 | 0.050 |
| 0.1 | 0.2 | 1.55 | 0.204 | — |
| 0.2 | 0.1 | 1.55 | 0.198 | 0.104 |
| 0.3 | 0.1 | 1.55 | 0.226 | — |
| 0.4 | 0.1 | 0.62 | 0.340 | — |

In the reaction of three and four moles of dichloramine B with one mole of aluminum chloride in carbon tetrachloride, there remained some unreacted dichloramine B after even thirty hours of heating. It was decided, therefore, in the study of this reaction to limit ourselves to two ratios of dichloramine B to aluminum chloride; specifically 2 : 1 and 1 : 1.

One of us has shown previously that anhydrous aluminum chloride reacts energetically with dichloramine B in the ratio of 1 : 1 in the medium of aromatic hydrocarbons, with formation of the corresponding oily complex and an equimolar amount of the chlorinated hydrocarbon.

Evidently, in case of carbon tetrachloride there is formed in the first stage of the reaction an unstable complex with the composition $C_6H_5SO_2\overset{+}{N}Cl\ \overset{-}{Al}Cl_4$ and, hence, for the normal course of the reaction it is necessary to take one mole of aluminum chloride per mole of dichloramine B.

With equimolar amounts of dichloramine B and aluminum chloride in an excess of carbon tetrachloride, all the dichloramine B and the aluminum chloride dissolved after but 30 minutes of heating to 34-35°. A heavy viscous light yellow oil collects on the bottom of the flask; this oil decomposes on further heating and evolves chlorine. This decomposition occurs particularly energetically at 50-52°.

Cyanuric chloride is formed in the reaction in addition to chlorine and benzenesulfonyl chloride. The quantitative isolation of these products permits the following summary equation to describe the reaction:

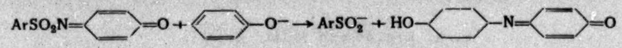
$$3C_6H_5SO_2NCl_2 + 3CCl_4 \rightarrow 3C_6H_5SO_2Cl + 6Cl_2 + C_3N_3Cl_3$$

The reaction is accompanied by the rupture of the bond between the atoms of nitrogen and sulfur.

Not a few such reactions are known among arylsulfonamides and their derivatives. For example, benzenesulfonodialkylamides yield about 70% of benzenesulfonyl chloride and dialkylsulfamic acid [1] on being heated with chlorosulfonic acid.

$$C_6H_5SO_2NR_2 + ClSO_3H \rightarrow C_6H_5SO_2Cl + R_2NSO_3H$$

It was established, by the studies made by S. N. Burmistrov and E. A. Titov [2] on the indophenol reaction of N-arylsulfonylquinonimines synthesized by them, that these compounds react, in an alkaline medium, with phenol with cleavage of the arylsulfonyl residue in the form of the anion of arylsulfinic acid.



Braun and Rudolph [3] showed that the decomposition of imido chlorides of the structure:

$$C_6H_5SO_2N=C(Cl)-R$$

is accompanied by the formation of benzenesulfonyl chloride and the corresponding nitrile. There are also known many examples of hydrolysis of sulfamide derivatives as the result of their being heated with acids [4], especially in the presence of phenols [5], which reactions lead to the formation of amines [6].

The course of the new reaction may be explained by considering the reaction of aluminum chloride with dichloramine B which is accompanied by evolution of chlorine.

$$ArSO_2NCl_2 + AlCl_3 \rightarrow ArSO_2\overset{+}{N}Cl\overset{-}{Al}Cl_4,$$
$$ArSO_2\overset{+}{N}Cl\overset{-}{Al}Cl_4 \rightarrow ArSO_2NClAlCl_2 + Cl_2.$$

The resulting aluminum compound derivative of dichloramine B reacts further with carbon tetrachloride:

$$ArSO_2NClAlCl_2 + CCl_4 \rightarrow ArSO_2NClCCl_3 + AlCl_3,$$
$$ArSO_2NClCCl_3 \rightarrow ArSO_2N{=}CCl_2 + Cl_2,$$
$$3ArSO_2N{=}CCl_2 \rightarrow 3ArSO_2Cl + C_3N_3Cl_3$$

The fact that dichloramine B reacts very readily with anhydrous aluminum chloride speaks in favor of this reaction scheme as does the evolution of chlorine which is observed in simple trituration of these substances in a mortar at room temperature.

In order to check this reaction mechanism there was run an experiment with heating of an equimolar mixture of dichloramine B with anhydrous aluminum chloride on a water bath. In this instance 0.7 mole of chlorine was evolved. No evolution of chlorine was observed during the further heating of the resulting product with carbon tetrachloride.

It appeared that this experiment neglects the above-shown reaction scheme. However, it is impossible to reject this scheme categorically since during the heating of dichloramine B with aluminum chloride in the presence of carbon tetrachloride the resulting aluminum derivative reacts, evidently, instantaneously, with the carbon tetrachloride.

Possibly in the presence of anhydrous aluminum chloride the dichloramine B reacts with carbon tetrachloride by means of free radicals with cleavage of chlorine:

$$CCl_4 \rightarrow CCl_3\cdot + Cl\cdot,$$
$$C_6H_5SO_2NCl_2 + CCl_3\cdot \rightarrow C_6H_5SO_2NClCCl_3 + Cl\cdot,$$
$$CCl_4 + Cl\cdot \rightarrow CCl_3\cdot + Cl_2,$$

$$C_6H_5SO_2NCl_2 + CCl_3\cdot \rightarrow C_6H_5SO_2NClCCl_3 + Cl\cdot \quad \text{etc.}$$
$$C_6H_5SO_2NClCCl_3 \rightarrow C_6H_5SO_2N{=}CCl_2 + Cl_2,$$
$$3C_6H_5SO_2N{=}CCl_2 \rightarrow 3C_6H_5SO_2Cl + C_3N_3Cl_3.$$

It should be indicated that benzenesulfonamide does not react with carbon tetrachloride under these conditions and that no evolution of chlorine occurs. A complex with the composition $C_6H_5SO_2NH_2 \cdot AlCl_3$ is obtained after the removal of carbon tetrachloride.

Benzenesulfonamide is always detected among the reaction products of N,N-dichlorobenzenesulfonamide with carbon tetrachloride in the presence of anhydrous aluminum chloride, besides the products mentioned above. The presence of this substance among the reaction products may be explained first by the presence of this material in the starting dichloramine and secondly by its formation from dichloramine B through a side reaction:

$$C_6H_5SO_2NCl_2 + 2HCl \rightarrow C_6H_5SO_2NH_2 + 2Cl_2.$$

The hydrogen chloride is always contained in anhydrous aluminum chloride as indicated by Thomas [7].

## EXPERIMENTAL

Into a flask with 500 ml capacity there was placed 150 ml of dry carbon tetrachloride, 26.6 g of aluminum chloride and 45.2 g of dichloramine B and the flask was provided with a reflux condenser. A homogeneous solution formed rapidly after the mixture had been stirred. The flask contents were slowly heated on a water bath with a simultaneous passage of dry air through the system for the displacement of the evolving chlorine. Chlorine was absorbed by 10% solution of sodium hydroxide. An energetic reaction occurred at 50-52° with violent evolution of chlorine. The temperature was raised gradually and the mixture was kept at reflux until the reaction was completed. The duration of the reaction was 4-5 hours. After completion of the reaction, carbon tetrachloride was decanted and the yellow oil which remained in the flask was washed with three portions (100 ml each) of carbon tetrachloride. The combined carbon tetrachloride solution was treated with ice water for the removal of aluminum chloride, was then filtered, dried with calcium chloride and freed of excess carbon tetrachloride by distillation. The residue was distilled in vacuum; benzenesulfonyl chloride distilled with cyanuric chloride in the range of 140-146° (at 25 mm). After their separation by filtration and extraction of cyanuric chloride from the condenser, there was obtained 14.2 g (40%) of benzenesulfonyl chloride and 2.7 g (22%) of cyanuric chloride with m.p. 144-145°.

Found %: Cl 57.20; N 22.44. M 183.4. $C_3N_3Cl_3$. Calculated %: Cl 57.67; N 22.79. M 184.4

Identification of benzenesulfonyl chloride was done by its conversion into benzenesulfonamide. The residue in the flask after the extraction with carbon tetrachloride was treated with ice water with acidification with hydrochloric acid for the removal of aluminum chloride. After drying and recrystallization from ethyl alcohol there was isolated 6.4 g (20%) of benzenesulfonamide; m.p. 152°. No depression was observed in the mixed melting point with pure benzenesulfonamide. The determination of the amount of chloride which had evolved during the reaction was made iodometrically and by the weight increment of the absorption flasks; both methods gave concordant results: 28.2 g (97.5%).

Experiments with doubled amount of dichloramine B in respect to aluminum chloride were run analogously. The duration of the reaction was 12-15 hours. The results of the experiments were approximately the same as with the equimolar ratio of dichloramine B and aluminum chloride, except for the fact that we failed to isolate any benzenesulfonamide in the pure state. There was isolated a product having double the molecular weight of benzenesulfonamide and the corresponding elemental composition. The results of the experiments are shown in Table 2.

We could not isolate cyanuric chloride in large amounts and its yield did not rise over 22-24%. The extraordinary volatility of cyanuric chloride and the losses associated with it constitute the cause of this result. It is sufficient to say that we found pure cyanuric chloride in the distilled benzenesulfonyl chloride as well as in crystalline state even in the tube used for chlorine take-off, despite the presence of a reflux condenser.

The low yield of benzenesulfonyl chloride may be explained by the fact that it forms a complex with aluminum chloride, which hydrolyzes forming benzenesulfonic acid during treatment with water.

$$C_6H_5SO_2Cl + AlCl_3 \longrightarrow C_6H_5\overset{+}{S}O_2\overset{-}{A}lCl_4$$

$$C_6H_5\overset{+}{S}O_2\overset{-}{A}lCl_4 + H_2O \longrightarrow C_6H_5SO_2OH + AlCl_3 + HCl$$

TABLE 2

| Starting materials | | Products obtained | |
|---|---|---|---|
| formula | amount (in g) | formula | yield (in %) |
| $C_6H_5SO_2NCl_2$ | 45.2 | $Cl_2$ | 95 |
| $AlCl_3$ | 13.3 | $C_6H_5SO_2Cl$ | 50 |
| $CCl_4$ | 240 | $C_3N_3Cl_3$ | 24 |
| | | $C_6H_5SO_2NH_2$ | 30 |

## SUMMARY

N,N-Dichlorobenzenesulfonamide reacts in carbon tetrachloride in the presence of anhydrous aluminum chloride, with formation of benzenesulfonyl chloride, cyanuric chloride and with evolution of chlorine according to the reaction schemes shown above. The reaction proceeds with the greatest rate with equimolar ratio of N,N-dichlorobenzenesulfonamide and aluminum chloride. Benzenesulfonamide always forms from side reactions and its yield rises with the use of a doubled amount of N,N-dichlorobenzenesulfonamide.

## LITERATURE CITED

[1] H. Suter, Chemistry of organic compounds of sulfur, Vol. 3, 40 (1951); Foreign Lit. Press.*

[2] S. I. Burmistov and E. A. Titov, J. Gen. Chem. 22, 999 (1952).**

[3] J. V. Braun and W. Rudolph, Ber. 67, 1762 (1934).

[4] H. Snyder and H. Geller, J. Am. Chem. Soc. 74, 4864 (1952).

[5] D. Weisblatt, B. Magerlein and D. Nyer, J. Am. Chem. Soc. 75, 3630 (1953).

[6] D. Klamann and G. Hofbauer, Ber. 86, 1246 (1953).

[7] C. Thomas, Anhydrous aluminum chloride in organic chemistry; p. 882 (1949); edited by Foreign Literature Press. *

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* Russian translation.

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# REACTION OF N,N-DICHLOROBENZENESULFONAMIDE WITH POLYHALOGEN DERIVATIVES OF METHANE. II.

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In our first paper we described the reaction of N,N-dichlorobenzenesulfonamide with carbon tetrachloride in the presence of anhydrous aluminum chloride [1].

N,N-Dichlorobenzenesulfonamide should react under analogous conditions with other polyhalogen derivatives of methane. In order to study this reaction, we set up some experiments with chloropicrin and chloroform.

Chloropicrin, which was both a reagent and the medium, was used in large excess in these experiments, while N,N-dichlorobenzenesulfonamide and aluminum chloride were taken in equimolar amounts. It turned out that heat evolution took place on mixing the reactants and an abundant evolution of chlorine occurred along with that of cyanuric chloride even under cooling to 5°.

It was proven by specially set-up experiments that no decomposition of chloropicrin, according to the equation $CCl_3NO_2 \rightarrow COCl_2 + NOCl$ takes place under these conditions under the influence of aluminum chloride.

It appeared that the evolution of nitrosyl chloride and phosgene occurs only on heating of chloropicrin with aluminum chloride almost to boiling.

After introduction of chloropicrin into the flask and cooling to 5°, there was added the aluminum chloride. No evolution of chlorine was observed. After the dissolution of aluminum chloride, the introduction of dichloramine B at 5° resulted in immediate evolution of chlorine and $ClNO_2$. After approximately three hours at 5° all the dichloramine had gone into solution. Bubbles of gases were continually formed in the flask in great abundance.

With gradual elevation of bath temperature to 30° the gas evolution became so abundant that foam appeared on the top of the mixture. A heavy yellow oil collected on the bottom of the flask. Under the conditions of the experiment the nitro group is cleaved from the molecule of chloropicrin and by joining an atom of chlorine forms a molecule of $ClNO_2$ which evolves along with chlorine. The $ClNO_2$ was isolated by us by its condensation in the liquid state.

Analysis of the alkali, through which the gaseous reaction products were passed for quantitative absorption, indicated the presence of the anion $NO_3^-$. Its presence was proved by six known qualitative tests, among them the microcrystalline reaction with "Nitron." The presence of $NO_3^-$ anion in the alkali may be connected only with the reaction:

$$NaOH + ClNO_2 \rightarrow NaNO_3 + HCl.$$

Consequently the isolation of $ClNO_2$ from the reaction of chloropicrin with dichloramine B cannot be doubted.

The separation and isolation of the reaction products gave a considerable amount of benzenesulfonyl chloride and a smaller amount of cyanuric chloride.

The found amounts of chlorine and $ClNO_2$ correspond to the following summary reaction equation:

$$3C_6H_5SO_2NCl_2 + 3CCl_3NO_2 \rightarrow 3C_6H_5SO_2Cl + C_3N_3Cl_3 + 3Cl_2 + 3ClNO_2.$$

It is possible that the process proceeds in several directions, since benzenesulfonyl chloride and cyanuric chloride were found in smaller amounts.

The reaction mechanism can be explained in this case quite easily by the formation of free radicals in the presence of aluminum chloride:

$$CCl_3NO_2 \longrightarrow CCl_3\cdot + NO_2\cdot$$
$$C_6H_5SO_2NCl_2 + CCl_3\cdot \longrightarrow C_6H_5SO_2NClCCl_3 + Cl\cdot$$
$$CCl_3NO_2 + Cl\cdot \longrightarrow CCl_3\cdot + ClNO_2$$
$$C_6H_5SO_2NCl_2 + CCl_3\cdot \longrightarrow C_6H_5SO_2NClCCl_3 + Cl\cdot \quad \text{etc.}$$

The resulting N-trichloromethyl derivative of dichloramine is unstable and decomposes with evolution of chlorine as in experiments with carbon tetrachloride [1].

$$C_6H_5SO_2NClCCl_3 \longrightarrow C_6H_5SO_2N{=}CCl_2 + Cl_2$$
$$3C_6H_5SO_2N{=}CCl_2 \longrightarrow 3C_6H_5SO_2Cl + C_3N_3Cl_3$$

Analogous experiments were run in chloroform medium.

It appeared that chloroform also reacts readily with dichloramine B with evolution of chlorine and a small amount of hydrogen chloride.

Among the reaction products there were found by us: benzenesulfonamide, benzenesulfonyl chloride and cyanuric chloride. The formation of chlorine, hydrogen chloride, benzenesulfonyl chloride and cyanuric chloride may be represented by the following equation:

$$3C_6H_5SO_2NCl_2 + 3CHCl_3 \longrightarrow 3C_6H_5SO_2Cl + C_3N_3Cl_3 + 3Cl_2 + 3HCl \qquad \text{(I)}$$

The formation of a considerable amount of benzenesulfonamide may be explained by the well-known reaction [2]:

$$C_6H_5SO_2NCl_2 + 2HCl \longrightarrow C_6H_5SO_2NH_2 + 2Cl_2 \qquad \text{(II)}$$

The other schemes for the formation of benzenesulfonamide:

$$C_6H_5SO_2NCl_2 + 2CHCl_3 \longrightarrow C_6H_5SO_2NH_2 + C_2Cl_6 + Cl_2 \quad \text{and}$$
$$C_6H_5SO_2NCl_2 + 2CHCl_3 \longrightarrow C_6H_5SO_2NH_2 + 2CCl_4$$

can be excluded since no hexachloroethane or carbon tetrachloride were found among the reaction products.

From Equations (I) and (II) we obtain the summary equation for the reaction between chloroform and dichloramine B in the presence of aluminum chloride:

$$9C_6H_5SO_2NCl_2 + 6CHCl_3 \longrightarrow 6C_6H_5SO_2Cl + 3C_6H_5SO_2NH_2 + 2C_3N_3Cl_3 + 12Cl_2 \qquad \text{(III)}$$

The reaction mechanism remains the same, evidently, as in the case of chloropicrin.

## EXPERIMENTAL

Reaction with chloropicrin. Into a flask, with 500 ml capacity, provided with a reflux condenser there was placed 107 g of dried and distilled chloropicrin. With constant cooling to 5° there was added 26.6 g of anhydrous aluminum chloride and 45.2 g of dichloramine B. The evolving chlorine and $ClNO_2$ were displaced from the flask by passage of dry air and were absorbed by 10% solution of alkali. After the dissolution of dichloramine B, the bath temperature was gradually raised from 0° to 30° and was kept at this level for eleven hours. The reaction was completed at bath temperature of 50° after cessation of chlorine evolution. The duration of the reaction was approximately 15 hours.

The weight gain in the absorption flasks was 27.57 g; the amount of chlorine found iodometrically was 14.12 g, and that of $ClNO_2$ found by difference was 13.45 g.

The excess chloropicrin was distilled in vacuum at bath temperature of 50°. The residue in the flask, which was a yellow oil, was subjected to a triple extraction with benzene (100 ml each) at 50°.

Benzenesulfonyl chloride, along with cyanuric chloride, was distilled at 16-18 mm in the range of 132-136°. After filtration from cyanuric chloride there was obtained 24.5 g of benzenesulfonyl chloride.

The residue in the flask, after extraction with benzene, was a dark substance which was then treated with ice water, filtered and dried. An additional amount of cyanuric chloride was removed from it by extraction with ether. In all 2.49 g of cyanuric chloride was isolated. The results of the experiments are shown in Table 1.

TABLE 1

| Starting and final products | Taken | Obtained | |
|---|---|---|---|
| | (in g) | (in g) | yield (in %) |
| $C_6H_5SO_2NCl_2$ | 45.2 | — | — |
| $AlCl_3$ | 26.6 | — | — |
| $CCl_3NO_2$ | 107 | — | — |
| $ClNO_2$ | — | 13.45 | 85 |
| $Cl_2$ | — | 14.12 | 100 |
| $C_6H_5SO_2Cl$ | — | 24.5 | 70 |
| $C_3N_3Cl_3$ | — | 2.49 | 33 |

TABLE 2

| Starting and final products | Taken | Obtained | |
|---|---|---|---|
| | (in g) | (in g) | yield (in %) |
| $C_6H_5SO_2NCl_2$ | 45.2 | — | — |
| $AlCl_3$ | 26.6 | — | — |
| $CHCl_3$ | 223 | — | — |
| $C_6H_5SO_2NH_2$ | — | 17.6 | 157 |
| $C_6H_5SO_2Cl$ | — | 7.07 | 30 |
| $Cl_2$ | — | 20.4 | 107 |
| $HCl$ | — | 0.2 | — |
| $C_3N_3Cl_3$ | — | 1.38 | 19 |

Reaction with chloroform. The technique of the experiments was the same as in the reaction with chloropicrin.

Into the flask there was introduced 150 ml of chloroform, 26.6 g of aluminum chloride and 45.2 g of dichloramine B. After termination of the intensive phase of the reaction at 35°, the reaction was brought to completion, i.e., cessation of chlorine evolution, by being gradually heated to the boiling point of the reaction mixture.

The oil remaining in the flask after the decantation of chloroform was extracted with three portions of chloroform of 100 ml each. After treatment with ice water and drying, there was isolated from it by fractional distillation at 23-24 mm at temperature interval of 140-143° the 7.07 g of benzenesulfonyl chloride and the 1.38 g of cyanuric chloride which were separated by filtration.

The total weight gain of the absorption flasks was 20.6 g; the amount of chlorine found iodometrically was 20.4 g, and that of hydrogen chloride found by difference was 0.2 g. The results of the experiment are shown in Table 2.

The residue in the flask after chloroform extraction was treated with ice water with acidification with hydrochloric acid; then it was filtered and recrystallized from water, yielding 17.6 g of benzenesulfonamide.

The yields of products were calculated according to the reaction Equation (III).

The excess yield of benzenesulfonamide and the decreased yield of benzenesulfonyl chloride and cyanuric chloride are of approximately the same magnitude and are explained by the same causes as in experiments with carbon tetrachloride [1].

## SUMMARY

N,N-Dichlorobenzenesulfonamide readily reacts with chloropicrin and chloroform, in the solutions in these substances, in the presence of anhydrous aluminum chloride, the reaction being in accord with the summary equations given above.

The reaction with chloropicrin proceeds readily in the temperature interval of 5-50° and that with chloroform at 35-60° with equimolar amounts of dichloramine B and aluminum chloride.

The mechanism of the reactions, which evidently proceed through free radicals, may be represented by the scheme shown above.

## LITERATURE CITED

[1] A. E. Kretov and M. M. Kremlev, J. Gen. Chem. 28, 1950 (1958).*

[2] H. Suter, Chemistry of organic compounds of sulfur, Vol. 3, 40 (1951), Foreign Literature Press.**

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# THERMOCATALYTIC TRANSFORMATIONS OF α-TERPINENE OVER GUMBRIN

V. V. Tishchenko and N. S. Lishenkova

Wallach observed the formation of terpinolene in the reaction of sulfuric acid with dipentene with its transformation, on further heating, into α-terpinene [1]. Later Venable showed that the action of activated floridin on dipentene leads to the same results [2]. Rudakov in repeating Wallach's experiments found that the action of small amounts of clay on dipentene at 160-170° causes the formation of terpinolene initially, and then that of α-terpinene. Among the final reaction products he found: $\Delta^{3}$-p-menthene, p-cymene and about 72% of polymers [3]. The formation of $\Delta^{3}$-p-menthene and p-cymene, evidently according to Rudakov, occurs as the result of conjugated hydrogenation of α-terpinene.

It appeared interesting to verify the correctness of this supposition since such an isomerization may have a close connection with the problem of origin and transformation of petroleum.

## EXPERIMENTAL

α-Terpinene was prepared by dehydration of terpineol with oxalic acid [4]. Cineol, formed along with α-terpinene in this reaction, was bound into a complex by two treatments with resorcinol, from which complex the α-terpinene was distilled in vacuum (7 mm) through a column with 40 theoretical plates. The isolated product had the following constants: b.p. 173-175° (760 mm), $d^{20}_{4}$ 0.8410, $n^{20}$D 1.4769. The nitrosite prepared according to Wallach's directions [5] melted at 155°.

Gumbrin (a clay of montmorillonite type) activated with hydrochloric acid was used as the catalyst for the thermocatalytic transformation of α-terpinene. The experiments were run in a round bottomed flask with a stirrer and a reflux condenser. The flask was immersed in an oil bath heated to 150-170°.

The conditions at which the polymerization of α-terpinene is reduced to a minimum were determined by preliminary experiments. It was shown that the polymerization depends first of all on the amount of the catalyst used in the experiment. The duration and the temperature in the experiment have only a secondary significance.

In the first experiments α-terpinene was heated with 1% of the catalyst at 150° for one hour. These conditions failed to produce any significant changes in the product, which after the experiment distilled within a narrow range, while the index of refraction changed only insignificantly.

The product obtained after the first such heating was again heated with a new portion of the catalyst (1%). However, the second heating did not cause a significant change of composition, as indicated by the distillation and the determination of the index of refraction, and it was impossible to prove the presence of any p-menthene and p-cymene in this material. The subsequent heating with a new portion of the catalyst for two hours gave a different result. The product (95.5 g) separated from the catalyst was separated by three distillations through a column with 20 theoretical plates at 5 mm into nine fractions each of which boiled within a 2° range. Density and index of refraction were determined for each fraction. Most interesting were the first and the ninth fractions whose constants approached closely to those of p-menthene and p-cymene.

1st fraction, b.p. 165-166° (760 mm), $d^{20}_{4}$ 0.8280, $n^{20}$D 1.4608.
9th fraction, b.p. 175-177° (760 mm), $d^{20}_{4}$ 0.8575, $n^{20}$D 1.4896.

The small volumes of the first (1.56 g) and the ninth (2.22 g) fractions hindered their study. In order to have them in sufficient amounts, the following experiment was set up. Terpinene (124.2 g) was heated for three hours at 170° with 3% of the catalyst. There was obtained 104.5 g (84.2%) of the catalyzate which was separated by three distillations at 7 mm into five two-degree fractions.

The first fraction (3.50 g) with b.p. 172-173°, $d^{20}_4$ 0.8296 and $n^{20}D$ 1.4610 approached very closely the constants for dihydrophellandrene or $\Delta^1$-p-menthene reported by Semmler [6] (b.p. 171-173°, $d^{20}$ 0.829, $n_D$ 1.4601).

Found %: C 87.20; H 13.15. M 137. $C_{10}H_{18}$. Calculated %: C 86.95; H 13.05. M 138.

$\Delta^1$-p-Menthene was determined in two samples of the first fraction by means of benzoyl hydroperoxide according to Nametkin [7]. Its content was found to be 96.75%.

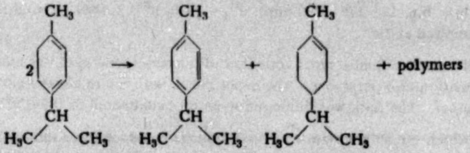
The fifth fraction (19.39 g) boiling at 175-176° (760 mm) and having $d^{20}_4$ 0.8561 and $n^{20}D$ 1.4896, corresponded to p-cymene.

Found %: C 89.65; H 10.25. M 135. $C_{10}H_{14}$. Calculated %: C 89.55; H 10.45. M 134.

Three g of the fifth fraction was oxidized with an alkaline solution of potassium permanganate according to Wiedman [8]. From the products of oxidation there was isolated terephthalic acid, whose basicity number was found to be equal to 1.92 by a titration with 0.1 N alkali. The solution remaining after the isolation of terephthalic acid was acidified and subjected to extraction with ether. The oil remaining after the distillation of ether solidified on standing into a crystalline mass from which there were isolated, after recrystallization from water, the long needles of p-hydroxyisopropylbenzoic acid, m.p. 155-156°.

The second, third and fourth fractions, boiling respectively at 49-50°, 50-51° and 51-52° (7 mm) and having $n^{20}D$ 1.4788, 1.4818 and 1.4862, were treated with the Beckmann mixture [9] in order to establish the presence of α-terpinene in them. The latter was discovered in noticeable amounts in the second and third fractions, while in the fourth fraction its presence was insignificant. These fractions evidently contain various mixtures of α-terpinene and p-cymene.

The formation of $\Delta^1$-p-menthene and p-cymene in these experiments may be explained by the following scheme:



The resulting polymers with $d^{20}_4$ 0.9358 had the following elemental composition.

Found %: C 88.56, 88.67; H 11.16, 11.27.

The molecular weight determined by the cryoscopic method was equal to 279. These results indicate that the polymers are represented by the diamer of α-terpinene.

## SUMMARY

The isomerization of the α-terpinene on gumbrin was studied at 150-170°. It was shown that α-terpinene isomerizes into $\Delta^1$-p-menthene and p-cymene as the result of disproportionation of hydrogen.

The polymers which are formed in the isomerization of α-terpinene consist of the dimer of terpinene.

## LITERATURE CITED

[1] O. Wallach, Lieb. Ann. 239, 15 (1887); 275, 109 (1893).

[2] C. S. Venable, J. Am. Chem. Soc. 45, 728 (1923).

[3] G. A. Rudakov, J. Gen. Chem. 10, 1673 (1940).

[4] D. V. Tishchenko and N. Summ, J. Gen. Chem. 22, 793 (1952).*

[5] O. Wallach, Lieb. Ann. 239, 36 (1893).

[6] F. Semmler, Ber. 36, 1035 (1903).

[7] S. S. Nametkin and L. Ia. Briusova, J. Gen. Chem. 27, 372 (1957).*

[8] O. Wiedman, and J. Baldin, Ber. 19, 583 (1886).

[9] A. Bayer, Ber. 27, 815 (1894).

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* Original Russian pagination. See C. B. Translation.

# THE COMPLEX – PYRIDINE-CUPROUS CHLORIDE – AS AN AUTOXIDATION CATALYST

## I. PREPARATION OF AZO COMPOUNDS FROM PRIMARY AROMATIC AMINES

A. P. Terent'ev and Ia. D. Mogilianskii

Azo compounds are often present among the numerous oxidation products of primary aromatic amines. Instances of catalytic effect of some substances on the oxidation of aniline by air have been described as the result of which more or less considerable amounts of azobenzene are formed [1-3]. However, owing to the not very high yields because of a number of side reactions, the reactions of oxidation of arylamines have not received a practical application for the preparation of azo compounds.

It was established by us that oxidation with air or gaseous oxygen of aromatic amines in pyridine solution in the presence of cuprous chloride does lead in a number of cases to smooth formation of azo compounds with a minimum amount of byproducts. Thus, p-azotoluene is obtained thereby in practically quantitative yield while its main bulk crystallizes directly from the reaction mixture owing to its low solubility in pyridine.

Oxidation by this method proceeds very smoothly for benzidine which yields a rather high yield of p,p'-diaminoazobiphenyl. Willstätter and Kalb [4] first prepared this compound in a 15% yield. The substance is isolated directly in a rather pure state in 72% yield by the technique described by us.

In case of other amines (aniline, p-anisidine) there is observed some tar formation, which is rather considerable if the reaction is run with heating. However, the side reactions are severely restricted by passage of pure oxygen at room temperature and by the use of more dilute solutions (about 11 ml of pyridine per 0.1 mole of amine) since in the concentrated solutions there occurs a considerable heat evolution of the mixture which aids tar formation.

The amount of cuprous chloride affects the yield of the azo compound but slightly. Thus, a 77% yield was obtained with the use of 0.8% of cuprous chloride in respect to the amount of the amine.

It was interesting to study the problem of the nature of the catalyst in this reaction and of the mechanism of its action. Insofar as the catalytic effect was discovered in a pyridine solution in the presence of cuprous chloride, it followed naturally that the significance of each of these components should be examined. With the example of p-toluidine we subjected to investigation the possibility of replacement of cuprous chloride by such salts as $FeCl_2$, $FeCl_3$, $CoCl_2$, $CuCl_2$, $Cu_2Br_2$ and $Cu_2I_2$. In all these cases the oxidation of amines was not observed at all; however, it began immediately after addition of cuprous chloride.

Also specific is the role of pyridine in this reaction since it cannot be replaced by alcohols, dioxane, dichloroethane or quinoline. In all these cases the oxidation of amines proceeds very slowly, while the amount of consumed oxygen exceeds but slightly the amount needed to oxidize the cuprous ion to cupric. However, after addition of pyridine the oxygen absorption becomes quite energetic.

On the basis of the above data we conclude that the active agent in this reaction of catalytic autoxidation is a complex of pyridine and cuprous chloride since the catalytic influence appears only in the presence of both substances simultaneously.

The effect of complex compounds of a series of metals on autoxidation of polyphenols, aromatic polyamines, thiols and other easily oxidizable compounds in aqueous medium had been studied by K. and Iu. Shibata

[5]. Two compounds $Cu_2Cl_2 \cdot 4Py$ and $Cu_2Cl \cdot 6Py$ were isolated for the first time and described by Lang [6]. The second of these compounds was isolated by us after dissolution of cuprous chloride in pyridine in a sealed ampoule with cooling of the solution. This complex is evidently the catalyst – oxygen carrier in the presently discussed reaction. As it was shown by us, a solution of cuprous chloride in pyridine absorbs 1 gram atom of oxygen per mole of cuprous chloride. The product of oxidation on being mixed with p-toluidine in nitrogen atmosphere gives up all the oxygen for dehydrogenation of the latter substance, being transformed itself into $Cu_2Cl_2 \cdot 6Py$ which fact was confirmed by analysis for chlorine content.

## EXPERIMENTAL

Oxidation of p-toluidine. Into a mixture of 12.5 g of p-toluidine (crystallized with 1 molecule of water), 20 ml of pyridine and 1.25 g of cuprous chloride there was passed at room temperature for two hours a stream of oxygen. Energetic gas absorption was observed along with a noticeable heat evolution. The precipitated scaly crystals (9.6 g) of p,p'-azotoluene were filtered off and washed with a small amount of dilute hydrochloric acid. From the mother liquor there was isolated an additional 0.4 g of p,p'-azotoluene (total yield 95%). After one recrystallization from alcohol the m.p. was 144°.

p-Hydrazotoluene. One g of the above prepared azo compound was dissolved in 100 ml of alcohol. After saturation of the solution with ammonia, hydrogen sulfide was passed into it. After some time there began the separation of colorless scaly crystals which became abundant after addition of a small amount of water. There was isolated 0.8 g of p-hydrazotoluene with m.p. 132-133° (from alcohol), which corresponds to the literature data.

The results of our experiments with some other amines are shown in the table.

| Expt. No. | Starting amine |  | Amt. of, pyridine (in ml) | Amt. of $Cu_2Cl_2$ (in g) | Azo compound obtained |  |  |  |
|---|---|---|---|---|---|---|---|---|
|  | Name | Amt. (in g) |  |  | Name | M. p. | Yield |  |
|  |  |  |  |  |  |  | in g | in % |
| 1 | Aniline | 9.3 | 20 | 1.25 | Azobenzene | 68° | 6.5 | 71.3 |
| 2 |  |  | 100 | 2.5 |  |  | 8 | 87.9 |
| 3 | p-Anisidine | 12.3 | 40 | 1.25 | 4,4'-Dimethoxy-azobenzene | 162 | 8.5 | 70 |
| 4 |  | 2.5 | 20 | 0.25 |  |  | 2 | 80 |
| 5 | 1,3,4-m-xylidine | 12 | 40 | 1.25 | 2,4,2',4'-Tetramethylazobenzene | 129 | 8 | 66.4 |
| 6 | Benzidine | 20 | 100 | 2 | 4,4'-Diaminoazobiphenyl | 285—286 | 14.5 | 72.5 |

Experiments 2 and 4 were run to clarify the effect of dilution.

The isolation of the azo compound shown in the table (except the last compound, which precipitated directly) was done by us in two ways: a) pyridine was distilled off in vacuum and the residue was extracted with ligroine; and b) after distillation of the major part of pyridine, dilute hydrochloric acid was added to the residue, thus dissolving the copper salts, and the crude product was extracted with ether which left behind a small black precipitate.

## Clarification of the Role of the Catalyst

a) Amount of oxygen absorbed by the catalyst. Into a small flask connected by a rubber tube to a gas burette there was placed 10 ml of pyridine and a carefully weighed amount of cuprous chloride. The flask was shaken mechanically until the absorption of oxygen stopped.

0.32, 0.64 g $Cu_2Cl_2$: 20.0, 40.0 ml $O_2$ (746 mm, 16°). Calculated: 19.9, 39.8 ml $O_2$ (calculated on 1 gram atom of oxygen per mole of cuprous chloride).

b) Transfer of oxygen. Cuprous chloride (0.96 g) in 15 ml of pyridine was saturated with oxygen. There was absorbed 60.5 ml (744 mm, 18°). The product of oxidation was transferred into an ampoule. After displacement of air by nitrogen, there was added 1 g of p-toluidine and the ampoule was sealed. Soon there was observed a change of color to dark orange and the formation of thin needle-like crystals. After two hours the ampoule was opened and to its contents there was added some dilute hydrochloric acid. The resulting orange precipitate was filtered off, washed with dilute hydrochloric acid and dried at 100-120°. There was isolated 0.5 g of p-azotoluene; calculated amount (on basis of oxygen) was 0.51 g of azotoluene.

Another analogous experiment was run for the purpose of isolation and study of the needle-like crystals which appear in the ampoule. The liquid was sucked from them in an atmosphere of hydrogen and the crystals were washed with a small volume of pyridine and were rapidly and thoroughly pressed on filter paper. A sample was transferred into a previously weighed container for determination of chlorine by the gravimetric method.

Found %: Cl 10.76. $Cu_2Cl_2 \cdot 6Py$. Calculated %: Cl 10.54.

## SUMMARY

1. Primary aromatic amines are oxidized by molecular oxygen in pyridine solution in the presence of cuprous chloride, forming azo compounds.

2. The catalyst in this reaction is a complex $Cu_2Cl_2 \cdot 6Py$, which adds oxygen readily and gives it up readily for dehydrogenation of the amine. Cuprous chloride cannot be replaced in this reaction by other salts, including copper salts. Replacement of pyridine by other solvents, as for example alcohol, dioxane, toluene, dichloroethane and quinoline, also gives negative results. The process proceeds most smoothly with pure oxygen at room temperature.

3. The present reaction may be used as a convenient method for the preparation of some azo compounds (p-azotoluene, p,p'-diaminoazobiphenyl, p,p'-dimethoxyazobenzene).

## LITERATURE CITED

[1] A. Terentieff, Bull. Soc. Chim. (4), 35, 1164 (1924).

[2] E. V. Alekseevskii and Z. E. Gol'braikh, J. Gen. Chem. 4, 934 (1934); Author's certificate 32499, 26 February 1933*; E. V. Alekseevskii and K. B. Frid, J. Gen. Chem. 15, 6 (1945).

[3] O. W. Brown and W. C. Frische, Ch. A. 42, 1793 (1948).

[4] R. Willstätter and L. Kalb, Ber. 38, 1238 (1905); 39, 3474 (1906).

[5] K. Shibata and Ju. Shibata, Katalytische Wirkungen der Metallkomplexverbindungen, Tokyo (1936).

[6] W. Lang, Ber. 21, 1578 (1888).

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* In Russian.

# INDOLE DERIVATIVES

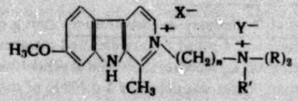
## V. SYNTHESIS OF BIS-QUATERNARY AMMONIUM SALTS OF HARMINE

N. F. Kucherov, V. P. Evdakov and N. K. Kochetkov

The reports concerning the physiological activity of unsymmetric bis-quaternary ammonium salts, which have appeared recently, [1-3] indicate certain possibilities which are opened by this class of compounds in the search for new gangliolytic and hypotensive preparations.

In this connection we have accomplished the synthesis of some compounds of this class, using as starting material the readily available alkaloid harmine. The compounds prepared by us may present a definite point of interest since, on one hand, it is specifically the bis-quaternary salts of β-carbolines that turned out to be active to the greater degree [1-3], while, on the other hand, harmine itself, as it is known, possesses some hypotensive action.

We prepared compounds of the general type as follows:

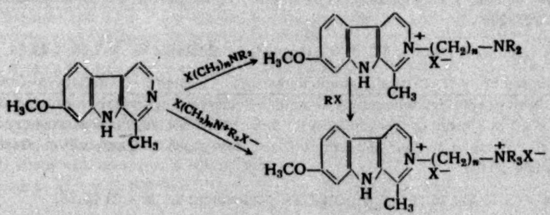


| | X | Y | R | R′ | n |
|---|---|---|---|---|---|
| (I) | I | I | $C_2H_5$ | $CH_3$ | 2 |
| (II) | Cl | Br | $C_2H_5$ | $C_2H_5$ | 2 |
| (III) | I | I | $CH_3$ | $CH_3$ | 2 |
| (IV) | I | I | $C_2H_5$ | $C_2H_5$ | 2 |
| (V) | Cl | I | $C_2H_5$ | $CH_3$ | 3 |
| (VI) | Cl | Br | $C_2H_5$ | $C_2H_5$ | 3 |
| (VII) | Br | Br | $C_2H_5$ | $C_2H_5$ | 4 |

In addition there was prepared, bythe reaction of harmine with ethylene bromide, the symmetric bis-quaternary salt – the dibromide of 1,2-bis(Py-N-1-methyl-7-methoxy-β-carbolinium)ethane (VIII), as well as the monoquaternary salt of harmine with benzyl chloride – the chloride of Py-N-benzyl-1-methyl-7-methoxy-β-carbolinium (IX).

The preparation of compounds (I)-(VII) was performed in two ways. The first variant of the synthesis consisted of the reaction of harmine with the appropriate dialkylaminoalkyl halide by heating in a mixture of toluene with nitrobenzene with the subsequent reaction of the resulting monoquaternary salt with an alkyl halide.

The second path consisted of the direct reaction of harmine with the corresponding ω-haloalkylammonium salt in boiling butyl alcohol or mixture of toluene with nitrobenzene with the direct formation of the bis-quaternary salt.



The yields of both methods varied within the limits of 54-74%. The bis-quaternary salts with n = 2 were prepared by the first method which turned out to be the more suitable method in this case since it eliminates the preparation of the ω-haloalkyl quaternary salt. However, the use of this method for the synthesis of compounds with n = 3 and n = 4 turned out to be impossible since under the relatively drastic conditions of the condensation, the dialkylaminopropyl halide and, especially, the dialkylaminobutyl halide are quite unstable and suffer an intra- or intermolecular condensation. Owing to this, the compounds with n = 3 and n = 4 were prepared by the second method. The ω-haloalkyl quaternary salts necessary for this were prepared by the recently described convenient method [4] or by the reaction of dialkylaminoalkyl halide with an alkyl halide.

The greatest experimental difficulties in the preparation of the compounds (I)-(VII) were connected with the very low solubility of harmine in the majority of organic solvents. The use of acetonitrile as the solvent, recommended by American authors [2] also failed to give the needed effect (the solubility of harmine even in this case was but 1 g per 250-270 ml of acetonitrile). Therefore, after a long search, we made use of a mixture of nitrobenzene with toluene and, although this combination still had its deficiencies, it did give the best results.

The compounds (I)-(VIII), prepared by us, as well as (VIII) and (IX) were tested at the Pharmacology Department of the Institute by D. A. Kharkevich. The results indicate that compounds (VIII) and (IX) are not interesting, that compounds (I)-(VII) do possess a hypotensive activity which agrees with the data on the bis-quaternary salts of the β-carboline series [3]. The compounds with n = 2 are the more active ones in respect to the depth and the duration of the hypotensive action; lengthening of the aliphatic chain to n = 3 or n = 4 lowers the hypotensive effect to a considerable degree. The greatest interest, among these compounds, is in compound (III) which while having the greatest hypotensive effect is also the least toxic one.

## EXPERIMENTAL

### Reaction of Harmine with Dialkylaminoalkyl Halides

**Chloride of Py-N-(2-diethylaminoethyl)-1-methyl-7-methoxy-β-carbolinium.** One g of harmine, 0.66 g of diethylaminoethyl chloride, 4 ml of anhydrous toluene and 4 ml of freshly distilled nitrobenzene were heated at reflux for 20 minutes, cooled, the precipitated crystals being separated, washed several times with small portions of acetone and recrystallized from 80% aqueous dioxane. There was obtained 1 g (62%) of the product with m.p. 204-206°.

Found %: N 11.87, 11.81; Cl 9.99, 9.96. $C_{19}H_{26}ON_3Cl$. Calculated %: N 12.07; Cl 10.19.

**Hydrochloride.** One g of the above substance was dissolved in anhydrous alcohol and treated with a methanolic solution of hydrogen chloride until a definitely acid reaction was produced. The precipitated crystalline mass was separated, washed with anhydrous alcohol and recrystallized from anhydrous alcohol. The yield was 0.85 g (77.2%); m.p. 257-259°. The literature data [5]: m.p. 252-253°.

Found %: C 59.10, 59.04; H 7.19, 7.24; Cl 18.33, 18.46. $C_{19}H_{27}ON_3Cl_2$. Calculated %: C 59.37; H 7.08; Cl 18.45.

**Di-iodide of Py-N-(2-diethylmethylammoniumethyl)-1-methyl-7-methoxy-β-carbolinium (I).** One g of the chloride of Py-N-(2-diethylaminoethyl)-1-methyl-7-methoxy-β-carbolinium and 0.96 g of potassium iodide in 60 ml of alcohol was refluxed for 1.5 hours on a water bath, filtered and the filtrate treated with 0.8 g of methyl iodide and the solution refluxed for 1.5 hours longer, cooled and filtered; the crystalline precipitate was washed with a small volume of alcohol and recrystallized from methanol. There was obtained 1 g (62%) of the product with m.p. 228-230°.

Found %: N 7.30, 7.29; I 43.49, 43.69. $C_{20}H_{29}ON_3I_2$. Calculated %: N 7.05; I 43.66.

**Chloride bromide of Py-N-(2-triethylammoniumethyl)- 1-methyl-7-methoxy-β-carbolinium (II).** One g of the chloride of Py-N-(2-diethylaminoethyl)-1-methyl-7-methoxy-β-carbolinium and 0.33 g of ethyl bromide were refluxed in 60 ml of alcohol on a water bath for three hours, cooled, the separated crystals filtered off, washed with a small volume of acetone and recrystallized from alcohol. There was obtained 0.9 g (69%) of product with m.p. 264-266°.

Found %: Br + Cl 25.02, 25.28. $C_{21}H_{31}ON_3ClBr$. Calculated %: Br + Cl 25.25.

**Di-iodide of Py-N-(2-trimethylammoniumethyl)-1-methyl-7-methoxy-β-carbolinium (III).** Reaction of 1 g of harmine with 0.5 g of dimethylaminoethyl chloride was run analogously to the synthesis of (I). There was obtained 0.9 g (60%) of the substance with m.p. 160-180° (with decomposition). To this product there was added 1.04 g of potassium iodide and 30 ml of methanol and the mixture was refluxed on a water bath for 40 minutes. The precipitated crystalline mass was separated, the filtrate was treated with 0.62 g of methyl iodide and the mixture heated at reflux on a water bath for one hour. The crystals were separated after cooling and were recrystallized from 85% alcohol. There was obtained 1.4 g (54%) of the substance with m.p. 236-238°.

Found %: I 45.18, 45.02. $C_{18}H_{25}ON_3I_2$. Calculated %: I 45.88.

**Di-iodide of Py-N-(2-triethylammoniumethyl)- 1-methyl-7-methoxy-β-carbolinium (IV).** From 1 g of the chloride of Py-N-(2-diethylaminoethyl)-1-methyl-7-methoxy-β-carbolinium, 0.96 g of potassium iodide and 1.5 g of ethyl iodide there was prepared the diiodide (IV) analogously to the diiodide (I). The yield was 1 g (64%); m.p. 234-236° (from water).

Found %: I 42.60, 42.33; N 7.00, 7.17. $C_{21}H_{31}ON_3I_2$. Calculated %: I 42.64; N 7.04.

## Reaction of Harmine with ω-Haloalkylammonium salts

**3-Chloropropyldiethylmethylammonium iodide.** To 5 g of 2-diethylaminopropyl chloride [6] there was added dropwise 4.6 g of methyl iodide in 25 ml of absolute ether and the mixture was refluxed for four hours, cooled, the crystalline mass separated, washed with absolute ether and used for the next step without purification.

Found %: I 43.49, 43.79. $C_8H_{19}NClI$. Calculated %: I 43.17.

**3-Chloropropyltriethylammonium bromide.** Thirty g of 1-chloro-3-bromopropane was heated on a water bath while 14.1 g of triethylamine in 50 ml of anhydrous benzene was added over one hour with stirring. The reaction mixture was stirred for 12 hours longer at room temperature. Benzene was distilled off in vacuum and the residue was dried with phosphorus pentoxide. There was obtained 16 g (54.9%) of hygroscopic substance with m.p. 105-110°.

Found %: Br 30.76, 30.59. $C_9H_{21}NClBr$. Calculated %: Br 30.92.

**1,4-Dibromobutane.** This was prepared from tetrahydrofuran by the method which was analogous to the known method of preparation of 1,5-dibromopentane [7]. The yield was 52%; b.p. 107-108° (55 mm), $n^{20}D$ 1.5189.

**4-Bromobutyltriethylammonium bromide.** This was prepared analogously to the 3-chloropropyltriethylammonium bromide from 30 g of 1,4-dibromobutane and 14 g of triethylamine. The yield was 23 g (52.2%); m.p. 110-120°. It was very hygroscopic.

Found %: Br 25.02, 24.98. $C_{10}H_{23}NBr_2$. Calculated %: Br 25.20.

**Py-N-(3-methyldiethylammoniumpropyl)-1-methyl-7-methoxy-β-carbolinium chloride iodide (V).** One g of harmine and 1.54 g of 3-chloropropylmethyldiethylammonium iodide in 25 ml of butyl alcohol were refluxed for 3 hours. The crystals were separated without cooling, washed with acetone and recrystallized from 80% aqueous acetone. There was obtained 1.1 g (62%) of the substance with m.p. 266-268°.

Found %: N 7.93, 8.14. $C_{21}H_{31}ON_3ClI$. Calculated %: N 8.33.

**Py-N-(3-triethylammoniumpropyl)-1-methyl-7-methoxy-β-carbolinium chloride bromine (VI).** The reaction of 1 g of harmine and 2.4 g of 3-chloropropyltriethylammonium bromide was run analogously to the preparation of (V). There was obtained 1.4 g (63%) of product with m.p. 268-270° (from 80% aqueous acetone).

Found %: N 8.79, 8.96; Cl + Br 24.32, 24.22. $C_{22}H_{33}ON_3ClBr$. Calculated %: N 8.92; Cl + Br 24.50.

**Py-N-(4-triethylammoniumbutyl)-1-methyl-7-methoxy-β-carbolinium dibromide (VII).** One g of harmine, 2.98 g of 4-bromobutyl triethylammonium bromide, 6 ml of freshly distilled nitrobenzene and 6 ml of anhydrous toluene were refluxed for 30 minutes. The crystalline mass which separated from the mixture was filtered off and washed several times with acetone. After recrystallization from 80% aqueous acetone there was obtained 1.9 g (77.6%) of product with m.p. 252-254°.

Found %: N 8.01, 8.13; Br 29.69, 29.89. $C_{23}H_{35}ON_3Br_2$. Calculated %: N 7.93; Br 30.19.

After running this reaction in acetonitrile with heating for 15 hours there was obtained (VI) in 60% yield.

### Reaction of Harmine with Ethylene Bromide and Benzyl Chloride

1,2-Bis-(Py-N-1-methyl-7-methoxy-β-carbolinium)ethane dibromide (VIII). In the reaction of 1 g of harmine and 0.88 g of ethylene bromide in a mixture of 4 ml of anhydrous toluene and 4 ml of freshly distilled nitrobenzene, under conditions analogous to those for the preparation of (VI) there was obtained 1.2 g (83.3%) of product with m.p. 254-256° (from 80% aqueous dioxane; melting with decomposition).

Found %: Br 25.86, 26.03. $C_{28}H_{28}O_2N_4Br_2$. Calculated %: Br 26.05.

Py-N-benzyl-1-methyl-7-methoxy-β-carbolinium chloride. From 1 g of harmine and 1.2 g of benzyl chloride there was obtained analogously to the above reaction 1.3 g (81.2%) of the product with m.p. 246-248° (with decomposition) after recrystallization from 80% aqueous dioxane and drying at 110-120°.

Found %: Cl 10.33, 10.29; N 8.60, 8.76. $C_{20}H_{19}ON_2Cl$. Calculated %: Cl 10.46; N 8.56.

Compound (VIII) has two melting points: 104-118° and 246-248°, since it crystallizes with one molecule of water, but loses the latter on being heated to 110-120°.

## SUMMARY

1. Two paths of synthesis were developed for unsymmetric bis-quaternary ammonium salts of the harmine series: a) reaction of harmine with dialkylaminoalkyl halides with the subsequent treatment of the product of the reaction with an alkyl halide, and b) reaction of harmine with ω-haloalkylammonium salts. The yields are are 55-75%.

2. The dependence of the hypotensive action on the structure in this series of compounds was discussed.

## LITERATURE CITED

[1] C. Cavallito, A. Gray and E. Spinner, J. Am. Chem. Soc. 76, 1862 (1954).

[2] A. Gray, E. Spinner, D. Schleiper and C. Cavallito, J. Am. Chem. Soc. 77, 3533 (1955).

[3] T. B. O'Dell, C. Luna and M. D. Napoli, J. Pharmacol. and Exper. Therapy, 114, 306 (1955).

[4] A. Gray and C. Cavallito, J. Am. Chem. Soc. 77, 3648 (1955).

[5] N. I. Koretskaia and A. V. Danilova and L. M. Utkin, J. Gen. Chem. 27, 542 (1957).*

[6] S. D. Torf, USSR Patent 36414, 11 July 1933.

[7] Synthesis of organic preparations, vol. 3, 112 (1952).**

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# β-AMINOVINYL KETONES

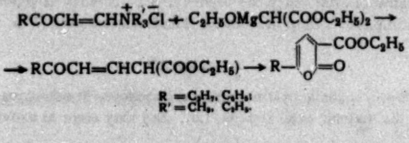
## IX. SALTS OF TRIALKYL-(γ-OXOALKENYL)-AMMONIUM AS OXOVINYLATING AGENTS

L. I. Kudriashov and N. K. Kochetkov

As it was recently shown in our laboratory [1], trialkyl-(γ-oxoalkenyl)ammonium chlorides are formed in high yields in the reaction of β-chlorovinyl ketones with tertiary amines. The properties of these compounds, which are interesting from the point of view of clarification of the general problem of interaction of a nitrogen atom with a carbonyl group in the molecule of β-aminovinyl ketone [2-4], remain almost unknown to this data. In the present paper we described briefly the results obtained in the study of the reaction of these quaternary salts with ethoxymagnesium malonic ester. This problem is of interest for the comparison of the behavior of our compounds with their saturated isologs – Mannich base haloalkylates. The latter are known to enter reactions with compounds which have a mobile hydrogen in the presence of bases. This reaction, known under the name of Mannich-Robinson reaction, is used widely at this time in organic chemistry for synthesis [5]. In addition, most recently there was examined the reaction of the salts of oxoalkenylammonium type with salts of hydrocyanic acid [6] and it was shown that in this reaction there occurs a replacement of the ammonium groupings by the nitrile group. This reaction is also, by its nature, one of the variants of the Mannich-Robinson reaction.

We hoped that salts of trialkyl-(γ-oxoalkenyl)ammonium type would be convenient in the preparative sense as oxovinylating agents, which would replace the β-chlorovinyl ketones, used by us previously for the synthesis of γ-oxoalkenylmalonic esters [7] and 6-alkyl-3-carbethoxy-α-pyrones [8]. We studied the condensation of triethyl-(β-butyroylvinyl)ammonium and triethyl-(β-benzoylvinyl)ammonium chlorides, as well as trimethyl-(β-butyroyl vinyl)ammonium chloride, with ethoxymagnesiummalonic ester. The latter was selected as the metallic derivative since in the case of sodiomalonic ester we failed to isolate from the reaction products of any individual compounds, which fact is evidently connected with some additional complications [8]. The reaction was run by addition of the solution of the quaternary salt to the solution of ethoxymagnesiummalonic ester in alcohol, i.e., under conditions which are close to those of Mannich-Robinson synthesis. The product of the initial oxovinylation reaction – the corresponding γ-oxoalkenylmalonic ester – was not isolated but was used directly for the cyclization into the derivative of pyrone by thermal cyclization or by action of acetyl chloride as described by us previously [8]. This was more convenient for the evaluation of the degree of progress of the reaction since in contrast to the isolation of pyrones, the isolation of γ-oxoalkenylmalonic esters is complicated by certain difficulties. The 6-alkyl-3-carbethoxy-α-pyrones prepared by us were identified by hydrolysis to the corresponding acids [9].

The results thus obtained showed that the condensation proceeds but that the yields are low. Thus, the condensation of the salt of triethyl-(β-benzoylvinyl)ammonium type gave 6-phenyl-3-carbethoxy-α-pyrone in a 48% yield, while the salt of triethyl-(β-butyroylvinyl)ammonium type gave 6-propyl-3-carbethoxy-α-pyrone in a yield of only 15%; replacement of the triethyl-(β-butyroylvinyl)ammonium salt by the trimethyl-(β-butyroylvinyl)ammonium salt did not change the result although this change did occur in the reaction of oxoalkenylammonium salts with cyanides [6].



$$\mathrm{RCOCH{=}CH\overset{+}{N}R'_3\overset{-}{Cl} + C_2H_5OMgCH(COOC_2H_5)_2 \longrightarrow RCOCH{=}CHCH(COOC_2H_5) \longrightarrow}$$

$R = C_3H_7,\ C_6H_5;$
$R' = CH_3,\ C_2H_5.$

It is evident that the results obtained by us are not of interest from the preparative viewpoint since it is more convenient to use β-chlorovinyl ketones for synthetic purposes [8, 9]. However, the reaction studied by us is interesting from the point of view of the principles, since it indicates that trialkyl-(γ-oxoalkenyl)ammonium salts, like haloalkylates of Mannich bases, are capable of exchange of their ammonium groups in typical reactions of nucleophilic substitution.

## EXPERIMENTAL

1. Reaction of triethyl-(β-butyroylvinyl)-ammonium chloride with ethoxymagnesiummalonic ester. In a three-necked flask, provided with a stirrer, a dropping funnel and a reflux condenser, there was prepared in the conventional manner a solution of ethoxymagnesiummalonic ester from 6.18 g of magnesium, 45 ml of malonic ester and 60 ml of anhydrous alcohol; the solution was cooled with ice water and treated over 30 minutes with stirring with the previously prepared solution of the quaternary salt (to the solution of 27.3 g of propyl β-chlorovinyl ketone in 10 ml of absolute ether there was added with cooling 30 ml of triethylamine and after 2 hours the solidified mass was dissolved in 50 ml of boiling alcohol), after which the cooling was stopped and the mixture was heated on a boiling water bath for 12 hours. The crystals of triethylamine hydrochloride which precipitated on cooling were rapidly filtered off on a glass filter (after drying, m.p. 252°), and the filtrate was evaporated in vacuum; to the residue there was added 40 ml of glacial acetic acid, then 150 ml of water, the precipitated oil was extracted with toluene (3 × 30 ml), the toluene extracts were washed with 50 ml of 10% acetic acid and with water (2 × 50 ml), the toluene was distilled off, the residue was refluxed for four hours with 100 ml of acetyl chloride, the acetyl chloride excess was distilled off and the residue was distilled, collecting the fraction with b.p. 148° (2 mm) to 195° (4 mm). A second distillation gave 6-propyl-3-carbethoxy-α-pyrone; yield: 6.4 g (14.6%); b.p. 145-148° (1 mm), $n^{20}D$ 1.5180.

6-Propyl-α-pyrone-3-carboxylic acid was obtained by hydrolysis of 6-propyl-3-carbethoxy-α-pyrone; m.p. 113° (from alcohol). Literature data [9]: m.p. 113°.

2. Reaction of trimethyl-(β-butyroylvinyl)ammonium chloride with ethoxymagnesiummalonic ester. To the solution of 18.8 g of propyl β-chlorovinyl ketone in 10 ml of absolute ether there was added dropwise at 0°, the liquid trimethylamine obtained from 30 g of the hydrochloride, dried by passage through a column packed with solid potassium hydroxide. The apparatus contained a trap with freezing mixture (acetone + dry ice) which permitted the return of the evaporating trimethylamine into the reaction zone. The reaction mixture was left for two hours at 0°, then allowed to come to room temperature and the residues of trimethylamine and ether were removed in vacuum. The quaternary salt obtained in this manner was dissolved in 30 ml of anhydrous alcohol and added to the solution of ethoxymagnesiummalonic ester (prepared from 4.5 g of magnesium and 39 ml of malonic ester in 50 ml of anhydrous alcohol), then refluxed for 14 hours; the main bulk of alcohol was distilled off, to the residue there was added with cooling 20 ml of glacial acetic acid and the mixture was worked up as described in the previous experiment. The yield of 6-propyl-3-carbethoxy-α-pyrone was 4.8 g (16%); b.p. 145-148° (1 mm), $n^{20}D$ 1.5173.

6-Propyl-α-pyrone-3-carboxylic acid was obtained by hydrolysis of 6-propyl-3-carbethoxy-α-pyrone; m.p. 113° (from alcohol).

3. Reaction of triethyl-(β-benzoylvinyl)ammonium chloride with ethoxymagnesiummalonic ester. To the solution of ethoxymagnesiummalonic ester (prepared from 2.4 g of magnesium, 18 ml of malonic ester and 33 ml of anhydrous alcohol) there was added dropwise with cooling by means of ice water over 30 minutes 8 g of triethyl-(β-benzoylvinyl)ammonium chloride in 18 ml of anhydrous alcohol; the water bath was then heated over one hour to boiling and the refluxing was continued for two hours. After cooling, there was added 20 ml of glacial acetic acid and 10 ml of water, the resulting precipitated oil was extracted with toluene (3 × 30 ml), the toluene extracts were washed with water (2 × 25 ml), the toluene was distilled off and all materials boiling under 106° (10 mm; with slight decomposition) were removed from the residue in vacuum on an oil bath; the flask residue was dissolved in 10 ml of methanol after which the 6-phenyl-3-carbethoxy-α-pyrone was precipitated by water. The yield was 3.51 g (48%); m.p. 105° (from methanol). The literature data [10]: m.p. 105-106°.

## SUMMARY

It was shown that trialkyl-γ-oxoalkenylammonium salts react with ethoxymagnesiummalonic ester, replacing the ammonium grouping by the malonic ester residue, i.e., they may serve as oxovinylating agents.

## LITERATURE CITED

[1] V. T. Klimko, A. Ia. Khorlin, V. A. Mikhalev, A. P. Skoldinov and N. K. Kochetkov, J. Gen. Chem. 27, 62 (1957).*

[2] N. K. Kochetkov, Progr. Chem. 24, 32 (1955).

[3] N. K. Kochetkov, Bull. Acad. Sci. USSR, ser. chem. 1954, 47.*

[4] N. K. Kochetkov and Ia. Dombrovskii, J. Gen. Chem. 26, 3081 (1956).*

[5] Organic Reactions, vol. 7, 146 (1956) (Russian edition).

[6] A. N. Nesmeianov and M. I. Rybinskaia, Doklady Akad. Nauk SSSR, 115, 315 (1957).*

[7] N. K. Kochetkov and L. I. Kudriashov, J. Gen. Chem. 26, 851 (1956).*

[8] N. K. Kochetkov and L. I. Kudriashov, J. Gen. Chem. 27, 248 (1957).*

[9] N. K. Kochetkov and L. I. Kudriashov, J. Gen. Chem. 28, 1511 (1958).*

[10] J. Walker, J. Chem. Soc. 1939, 120.

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# SYNTHESIS OF THEOPHYLLINE AND CAFFEINE FROM UREA AND SODIUM CYANOACETATE

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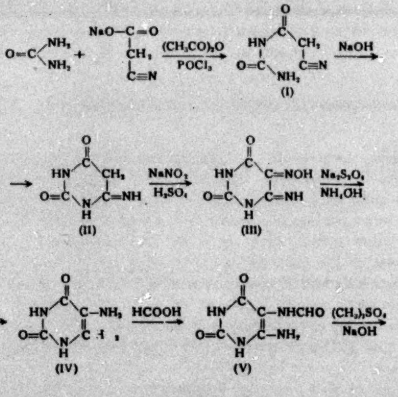
The synthesis of theophylline (VII) and caffeine (VIII) from dimethylurea and cyanoacetic acid was performed for the first time by Traube [1]. In its initial form this method had only a theoretical interest. Later it was improved considerably by other workers [2-10]. However, the practical utilization of Traube's method was hindered by the fact that difficultly obtainable symmetric dimethylurea was used as the starting material for the synthesis of theophylline and caffeine. Gapner and Kreps [4] realized the synthesis of these compounds from methylurea, but this did not make the Traube method any more usable in the practical sense since monomethylurea still remains a difficultly accessible material. Bobranski and Synowiedski [5] replaced dimethylurea by urea in the preparation of theophylline and caffeine. The introduction of methyl groups into the pyrimidine or the imidazole rings of the above compounds was realized by these workers through methylation of the intermediate reaction products. For preparation of theophylline the iminobarbituric acid (II) was subjected to methylation, while for the preparation of caffeine, the formyl derivative of 4,5-diaminouracil (V) was methylated. An attempt to use the formyl derivative (V) for the preparation of theophylline as well, made by these authors, failed.

In working on the study of the methods of preparation of theophylline and caffeine, we studied in detail the process of methylation of the formyl derivative of 4,5-diaminouracil (V). Here it was established that methylation of compound (V) by two moles of dimethyl sulfate, taken in slight excess at 25-27° and pH 8.5-9 gave 1,3-dimethyl-4-amino-5-formylaminouracil (VI) in almost quantitative yield.* This permitted us to realize the synthesis of theophylline and caffeine according to the scheme shown below:



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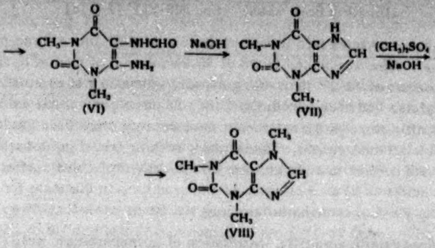
* According to the German patent [11], the formyl derivative of 4,5-diaminouracil is methylated to 1,3-dimethyl-4-amino-5-formylaminouracil by means of methyl iodide under pressure.



As it is evident from this scheme, cheap urea and sodium cyanoacetate are used as the starting materials for the synthesis. In case of the preparation of caffeine (VIII), theophylline (VII) becomes an intermediate product of the synthesis.

In completion of this work, besides the study of the process of methylation of the formyl derivative of 4,5-diaminouracil, we studied the methods of preparation of various intermediate products of synthesis of theophylline. As the result of this the yields were considerably improved and the quality of the intermediate products was improved.

Nitrosation of iminobarbituric acid (II) was run precisely under the conditions described in the literature [12].

The preparation of cyanoacetylurea (I) – the first intermediate product in the synthesis of theophylline – was run by us according to the method of Hepner and Frenkenberg [3], which these authors had used in the preparation of phenylmethylcyanoacetylurea. This permitted us to prepare cyanoacetylurea of good quality in yields of 82-84%.

Cyclization of cyanoacetylurea (I) into iminobarbituric acid (II) was run in a solution of sodium hydroxide. Several methods of cyclization of cyanoacetylurea into iminobarbituric acid have been described in the literature [1, 5, 12]. During the experimental verification it appeared that none of them afford a product of good quality in a satisfactory yield. The best yield of iminobarbituric acid (II) was obtained by us in the treatment of cyanoacetylurea (I) for three hours with 40% solution of sodium hydroxide at 25°.

Reduction of iminovyaluric acid to 4,5-diaminouracil was performed with sodium hydrosulfite according to the technique which was used by Bogert and Davidson [13] for the reduction of 5-nitrouracil.

Considerable improvements were also made in the stages of preparation of the formyl derivative of 4,5-diaminouracil, the sodium salt of theophylline and its isolation from the reaction mixture.

All this permitted us to increase very considerably the yield of theophylline and caffeine. In calculation on the initial sodium cyanoacetate, the yield of theophylline was 50%. In methylation of the sodium salt of theophylline with dimethyl sulfate there was obtained a 94-95% yield of caffeine.

## EXPERIMENTAL

Preparation of cyanoacetylurea (I). In a three-necked flask with ground glass joints, provided with a stirrer, thermometer and a condenser, there was placed 90 g of 40% (or 36 g 100%) well dried sodium cyanoacetate and 40 ml of glacial acetic acid. To the resulting thick mixture there was added with stirring 10 ml of phosphorus oxychloride. The reaction mixture liquefied during this operation and the temperature rose to 50-60°. After addition of the entire amount of the phosphorus oxychloride at 50°, there was added 20 g of urea and 55 ml of acetic anhydride. (During the addition of acetic anhydride a small exothermic effect is observed sometimes). The contents of the flask were heated to 65-67° and kept at this temperature for two hours. Then the stirrer was replaced by a capillary tube and the reflux condenser by a downward condenser, after which the mixture of acetic anhydride and acetic acid was distilled in vacuum at a temperature not more than 67°. To the remaining solid residue there was added 100 ml of water and, after one hour's standing and replacing the capillary tube by the stirrer, the reaction mixture was stirred until a homogeneous suspension resulted. The undissolved precipitate of cyanoacetylurea was filtered off and washed thoroughly with water until the acid test to litmus disappeared. The resulting product was dried at 100-110°. The yield of cyanoacetylurea was 35.9 g (84.1%). The m.p. of the technical grade product was 203-206°. After recrystallization from water: m.p. 208-211° [14, 15].

Cyclization of cyanoacetylurea into iminobarbituric acid (II). Into a three-necked flask, provided with a stirrer and a thermometer, there was placed 90 ml of 40.9% solution of sodium hydroxide and over one hour at a the temperature not in excess of 20-25° there was gradually added 30 g of cyanoacetylurea with m.p. 200-203°. After all the cyanoacetylurea had been added, the flask contents were maintained at 20-25° for 2.5 hours. The initially thick and difficultly stirrable heterogeneous mass became more fluid gradually and at the end of the treatment it was completely homogeneous. The resulting sodium salt of iminobarbituric acid was neutralized with 1:1 hydrochloric acid with cooling to a neutral test with Bromthymol blue. After 3-5 hours standing, the precipitated iminobarbituric acid was filtered off, pressed well and used in this state for the conversion to iminovyaluric acid, considering that the yield of iminobarbituric acid was theoretical, i.e., 30 g.

Preparation of iminovyaluric acid (III). Nitrosation of iminobarbituric acid (II), prepared in the preceding experiment, was run by the technique of Biltz and Schmidt [12]. From 30 g of compound (II) there was obtained 35.6 g (84.8%) of the sodium salt of iminovyaluric acid.

Reduction of iminovyaluric acid to 4,5-diaminouracil (IV). To the suspension of 35.6 g of sodium salt of iminovyaluric acid in 560 ml of water there was added 24.6 ml of 19.7% solution of ammonia and 172 g of sodium hydrosulfite (the medium was basic to phenolphthalein). After addition of the sodium hydrosulfite, the reaction mixture was heated on a water bath at 55° for 15 minutes, after which the bath was heated to boiling and the reaction mixture was kept on the boiling water bath for ten minutes. The reaction mixture became totally colorless. The resulting precipitate was filtered off, after cooling to 10°, washed with water to remove all odor of sulfur compounds and dried at 60-70°. The yield of technical grade (96%) 4,5-diaminouracil was 28.6 g (96.8%).

Preparation of 4-amino-5-formylaminouracil (V). To the suspension of 28.6 g of 4,5-diaminouracil in 200 ml of water there was added 17 ml of 85% formic acid. The resulting mixture was refluxed for one hour, after which it was allowed to stand for two hours at room temperature. The resulting precipitate of the formyl derivative was filtered off, washed with water and dried at 60-70°. The yield was 31.6 g (91.3%).

Preparation of theophylline (VII). a) Methylation of the formyl derivative of 4,5-diaminouracil. The formyl derivative of 4,5-diamonouracil (31.6 g) was suspended in 190 ml of water. To the resulting suspension there was added with energetic stirring 54.6 g of dimethyl sulfate in one portion after which 72 ml of 6 N solution of sodium hydroxide was added gradually, maintaining the pH of the solution at 8.5-9 during the process of methylation at 25-27°. The addition of alkali usually required 60-75 minutes. The formyl derivative of 4,5-diaminouracil passed partially into solution during the methylation process and simultaneously with this there occurred the precipitation of the methylated product. At times a complete solution of the precipitate was observed and the solution remained clear for 10-15 minutes after which a rapid thickening of the reaction mixture occurred. A colorless precipitate (needles) of 1,3-dimethyl-4-amino-5-formylaminouracil formed. After the consumption of alkali had terminated (for 5-10 minutes the pH of the medium remained without change), the mixture was kept at 25-27° for one hour, adding (in case of disappearance of the alkaline reaction to phenolphthalein) an additional amount of alkali. Usually after one hour's stirring, the pH of the medium does not change.

b) Transformation of the formyl derivative of 1,3-dimethyl-4,5-diaminouracil into theophylline. To the reaction mixture obtained in the preceding experiment there was added 31.6 ml of 6 N solution of sodium hydroxide, 71 g of sodium chloride and the solution was heated on a water bath. At 45-50° there took place a complete dissolution of the precipitate, while at 55-60° there began to precipitate the sodium salt of theophylline. The reaction mixture was kept for ten minutes at 80-95° and allowed to stand for 10-12 hours. The precipitate of the sodium salt of theophylline was filtered off after cooling of the reaction mixture to 10°, and was washed with a saturated solution of sodium chloride, after which it was dissolved in 400 ml of water with heating on a boiling water bath. Carbon was added to the resulting solution and after 15 minutes of heating on a boiling water bath the mixture was filtered. To the hot colorless solution there was added with stirring 100 g of sodium chloride. Sodium salt of theophylline precipitated and this, after 2-3 hours of standing at room temperature, was cooled to 10°, filtered, pressed well on the filter and suspended in 25 ml of water. The resulting suspension was neutralized with 25 ml of hydrochloricaacid (1:1) until neutral to Bromthymol blue and to Congo red. The resulting colorless precipitate of theophylline was filtered off after 3-4 hours standing at room temperature and dried at

120-125°. The weight of theophylline was 29 g (92%); m.p. 263-265°. After recrystallization from 5-6 parts of water, the weight was 26 g (82%); m.p. 268-170° (mixed m.p. with authentic theophylline was 269-270°).

Found %: N 31.16. $C_7H_8O_2N_4$. Calculated %: N 31.09.

Methylation of theophylline to caffeine (VIII). Into a three-necked flask, provided with a stirrer, a thermometer and a reflux condenser, there was placed 20 g of theophylline, 60 ml of water and 15 ml of 32.2% solution of sodium hydroxide. The flask contents thickened considerably during this operation. To the resulting sodium salt of theophylline there was gradually added with intensive stirring 11.8 ml of dimethyl sulfate, maintaining the temperature of the reaction mixture during methylation within 32-35°. The precipitate of the sodium salt of theophylline dissolved completely toward the end of methylation and almost immediately the caffeine precipitated. The reaction mixture was kept at 40-45° for one hour, maintaining the alkaline reaction to Bromthymol blue, after which it was heated to 90° and left at room temperature for 5-10 hours. The reaction mixture was then cooled to 5°-0°, the precipitate of caffeine was filtered off, washed on the filter with a small volume of ice water and dried at 110-120°. The weight of dry caffeine was 20.4 g. The m.p. of the technical grade product was 231-233°. After recrystallization from 3 parts of water with addition of activated charcoal, there was obtained 18.6 g of pure caffeine with m.p. 232-235°. From the mother liquor and the filtrate from the recrystallization there was obtained by extraction and a subsequent purification an additional 1.6 g of pure caffeine. The total yield of caffeine was 20.2 g (94%). The mixed m.p. with authentic caffeine was 232-234°.

## SUMMARY

1. Theophylline and caffeine were prepared in 50% yield from urea and sodium cyanoacetate. The synthesis of these compounds was done by one reaction scheme.

2. The methods of preparation of intermediate products in the synthesis of theophylline – cyanoacetylurea, iminobarbituric acid etc. – were improved. The possibility of methylation of the formyl derivative of 4,5-diaminouracil with dimethyl sulfate in an alkaline medium to 1,3-dimethyl-4-amino-5-formylaminouracil was indicated.

## LITERATURE CITED

[1] W. Traube, Ber. 33, 3035 (1900).

[2] F. Baum, Ber. 41, 530 (1908).

[3] B. Hepner and S. Frenkenberg, Helv. Chim. Acta. 15, 352 (1932).

[4] B. Hepner and L. Kreps, J. Gen. Chem. 16, 179 (1946); Chem. Abstr. 41, 96 (1947).

[5] B. Bobranski and Z. Synowiedski, J. Am. Pharm. Ass. 37, 62 (1948); Chem. Abstr. 42, 4123 (1948).

[6] German Patent 138,444; Chem. Zentr. 1903, I, 370.

[7] U. S. Patent 2,523,496; Chem. Abstr. 45, 6657 (1951).

[8] U. S. Patent 2,564,351; Chem. Abstr. 46, 2574 (1952).

[9] Canadian Patent 497,928; Referat. Zhur. Khim. 1955, 15100.

[10] U. S. Patent 2,646,432; Chem. Abstr. 48, 8819 (1954).

[11] German Patent 148,208; Chem. Zentr. 1904, I, 618.

[12] H. Biltz and W. Schmidt, Lieb. Ann. 431, 94 (1923).

[13] M. T. Bogert and D. Davidson, J. Am. Chem. Soc. 55, 1667 (1953); Helv. Chim. Acta. 15, 350 (1932).

[14] W. Traube, Ber. 33, 1381 (1900).

[15] M. Conrad and A. Schulze, Ber. 42, 741 (1909).

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# PREPARATION OF THEOPHYLLINE AND CAFFEINE FROM URIC ACID

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Several methods of preparation of caffeine (VI) and theophylline (V) from uric acid (I) have been described in the literature.

In 1899-1901 the workers of the Bayer firm had accomplished the transformation of uric acid into 8-methylcaffeine [1, 2]. In chlorination of 8-methylcaffeine [3, 4] and the subsequent hydrolysis of the tri- and tetra-halo derivatives formed thereby [5], there occurs a removal of one or two methyl groups and, accordingly, there is formed either caffeine or theophylline. E. Fischer prepared 8-chlorocaffeine from uric acid [6-8], the former being used subsequently for the preparation of theophylline [9-11] and other derivatives of xanthine.

In 1950-1953 Bredereck and co-workers published several papers on the utilization of uric acid for the preparation of caffeine, theophylline and other derivatives of xanthine. According to the data obtained by these authors, xanthine is formed on heating uric acid with formamide, while methylation of xanthine with dimethyl sulfate in an alkaline medium yields caffeine [12]. In later papers [13, 14] Bredereck and co-workers used the triacetyl derivative of 4,5-diaminouracil as an intermediate product for the preparation of caffeine and theophylline, this intermediate being prepared by them by the reaction of uric acid with acetic anhydride in the presence of pyridine.

Only one of the published methods from the literature has found a practical application for the preparation of theophylline and caffeine from uric acid, this method utilizing 8-methylcaffeine as an intermediate product. However even this method has material defects, despite the improvements developed by I. T. Strukov and L. S. Diskina [15], as well as E. S. Golovchinskaia [16], the defects which prevent the wide use of uric acid for the preparation of the indicated products. At the same time the use of uric acid for an industrial synthesis of medicinal agents of the purine series has a first rate importance since uric acid is an available product and may be obtained in any amount from the wastes of poultry husbandry — hen manure.

In a search for a simpler method of preparation of caffeine and theophylline we started with 4,5-diacetylaminouracil (II), the method of preparation of which from uric acid had been developed by the present authors [17]. Substance (II) on treatment with alkali may cleave one or two acetyl groups and be transformed into 4-amino-5-acetylaminouracil (VII) or into 4,5-diaminouracil (VIII).

Several methods of hydrolysis of 4,5-diacetylaminouracil (II) to the monoacetyl derivative [13, 18] and 4,5-diaminouracil [13, 19] are known. During the experimental verification it was established that all of them yield final products of poor quality and, owing to this, are unsuitable for practical utilization.

A detailed study of the conditions of hydrolysis of the diacetyl derivative (II) showed that the acetyl group in position 4 is especially readily cleaved. On heating 4,5-diacetylaminouracil on a water bath for one hour with a dilute solution of aqueous ammonia (approximately 0.9 N) used in slight excess over the theoretical amount, there is formed 4-amino-5-acetylaminouracil (VII) in yield of 93-95% [20]. On heating 4-amino-5-acetylaminouracil on a water bath for two hours with 6-10 N solution of sodium hydroxide, both acetyl groups are cleaved and there is obtained 4,5-diaminouracil, which is isolated from the reaction mixture in the form of its sulfate (VIII) on acidification with sulfuric acid.

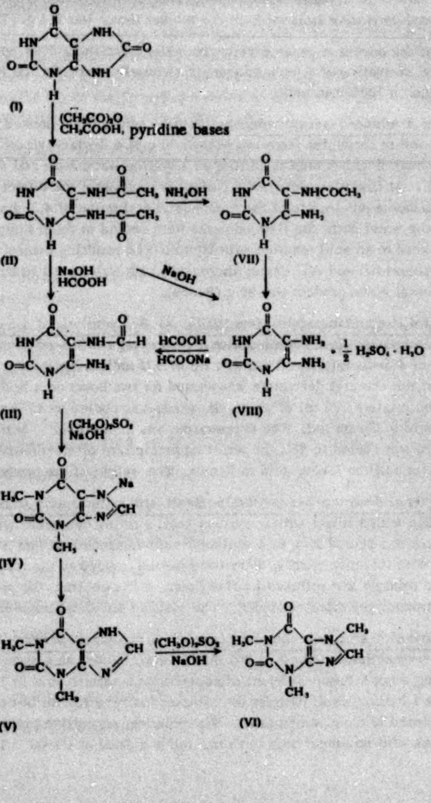
4,5-Diaminouracil may also be obtained from the monoacetyl derivative (VII). In contrast to the diacetyl derivative (II), which is hydrolyzed to 4,5-diaminouracil only in alkaline medium, the monoacetyl derivative

(VII) may be hydrolyzed to 4,5-diaminouracil not only in alkaline but also in acidic medium [13].

As shown by our experiments, the monoacetyl derivative (VII) is hydrolyzed by a solution of sulfuric acid in methyl alcohol; hereby there is formed the acid sulfate of 4,5-diaminouracil with yields of 93-95%. A somewhat lower yield of the sulfate of 4,5-diaminouracil (VIII) is obtained after a brief heating (10-15 minutes) of the monoacetyl derivative with a large excess of 2 N aqueous solution of sulfuric acid on a water bath.

The sulfate of 4,5-diaminouracil (VIII) obtained through the use of the alkaline or the acidic hydrolysis, is converted into the formyl derivative of 4,5-diaminouracil (III) by heating with an aqueous solution of sodium formate and a small amount of formic acid. This compound (III) yields the sodium salt of theophylline (IV) on methylation with dimethyl sulfate and a subsequent cyclization in an alkaline medium [21].

Duration the preparation of the formyl derivative of 4,5-diaminouracil (III) there is no necessity for the isolation of the sulfate of 4,5-diaminouracil. If the reaction mixture formed after the hydrolysis of the diacetyl derivative with sodium hydroxide is acidified with formic acid and the resulting mixture is boiled for one hour, the end product of the reaction is the formyl derivative of 4,5-diaminouracil (III). The excess alkali after the hydrolysis may be also neutralized with hydrochloric acid and the formic acid added only in an amount needed for the formylation of the 4,5-diaminouracil. The entire process of transformation of uric acid into theophylline and caffeine may be shown by the following scheme:



In working along this scheme the yield of theophylline reaches about 45-46% calculated on the original uric acid. The yield of caffeine in methylation of theophylline with the dimethyl sulfate reaches 90-94%.

## EXPERIMENTAL

Preparation of diacetyl derivative of 4,5-diaminouracil (II). Into a three-necked round bottomed flask with ground glass joints, with 750 ml capacity, provided with a stirrer, a thermometer and a reflux condenser, there was placed 100 g of 92-95% uric acid, 150 ml of acetic anhydride, 180 ml of acetic acid (glacial) and 100 ml of pyridine bases boiling in the interval of 126-138°. The flask contents were refluxed, with constant stirring, on an oil bath (the bath temperature was 155-160°) until the cessation of evolution of carbon dioxide, which was completed after 3.5-4 hours. To the reaction mixture was added 10 ml of water and the heating was continued for 30 minutes. The resulting diacetyl derivative of 4,5-diaminouracil was filtered off after cooling, thoroughly pressed free of mother liquor, suspended in 130-150 ml of water and refiltered. This operation was repeated twice. The thus washed product was dissolved without drying in 22.5 fold (relative to the weight of uric acid) amount of water with heating and the mixture was filtered from the water insoluble 8-methylxanthine. To the filtrate there was added 2 g of activated carbon, the solution was boiled for 3-5 minutes and filtered once again. The filtrate was cooled to 5-10° and the precipitated diacetyl derivative was filtered off and dried at 100-120°. Its weight was 84 g. The mother liquor, obtained from the crystallization of the diacetyl derivative, was evaporated on a water bath until crystallization began. The precipitate was filtered off and dried at 100-120°. The weight of the diacetyl derivative isolated from the mother liquor was 9.4 g. The total yield was 93.4 g (75%).

The weight of dry technical grade 8-methylxanthine containing 60% pure product was 14.8 g. Thus, the yield of the diacetyl derivative of 4,5-diaminouracil (with allowance for the 8-methylxanthine obtained) is about 85% calculated on 100% uric acid.

Preparation of 4-amino-5-acetylaminouracil (VII). Into a three-necked flask provided with a stirrer, a thermometer and a reflux condenser there was placed 30 g of 4,5-diacetylaminouracil and 120 ml of water. The flask contents were heated with intensive stirring on a boiling water bath and 60 ml of 2.5 N aqueous ammonia was added at 93-95°. At first there occurred a complete solution of the diacetyl derivative of 4,5-diaminouracil, after which there formed a precipitate of the monoacetyl derivative of 4,5-diaminouracil. After one hour of heating on the boiling water bath, the flask contents were cooled to room temperature and acidified with dilute (1:1) hydrochloric acid to an acid reaction with litmus. The resulting precipitate of the monoacetyl derivative of 4,5-diaminouracil was filtered off, washed thoroughly with water until neutral to litmus and dried at 100-120°. The weight of technical grade product was 20 g (94.5%).

Preparation of 4,5-diaminouracil sulfate (VIII). a) By hydrolysis of 4,5-diacetylaminouracil (II) in alkaline medium. Into a three-necked flask provided with a stirrer and a reflux condenser there was placed 30 g of the diacetyl derivative of 4,5-diaminouracil and 180 ml of 6 N sodium hydroxide. The resulting transparent solution of the sodium salt of the diacetyl derivative was heated for two hours on a boiling water bath. Then, there was added to the reaction mixture 180 ml of water, the whole was cooled to 40° and neutralized with 28 ml of 1:1 sulfuric acid until acid to Congo red. The temperature was maintained below 50° during the neutralization. The reaction mixture was cooled to 25°, the resulting precipitate of 4,5-diaminouracil sulfate was filtered off and washed with water until no longer acid to litmus. The weight of the product, dried at 60-70°, was 24 g (87%).

b) By hydrolysis of 4-amino-5-acetylaminouracil with sulfuric acid in methyl alcohol. Into a three-necked flask, provided with a stirrer with a mercury seal, a reflux condenser with a calcium chloride tube and a dropping funnel, there was placed 23 g of 4-amino-5-acetylaminouracil and 230 ml of methyl alcohol dried over unquenched lime. With intensive stirring there was gradually added to the resulting suspension 23 ml of concentrated sulfuric acid and the mixture was refluxed for five hours. After cooling, the precipitate was filtered off, washed several times with alcohol and dried at 50-60°. The yield of 4,5-diaminouracil acid sulfate was 27.8 g (93%).

c) By hydrolysis of 4-amino-5-acetylaminouracil with aqueous solution of sulfuric acid. To a suspension of 15 g of 4-amino-5-acetylaminouracil in 750 ml of water, heated on a water bath to 93-95°, there was added with intensive stirring a hot solution of 56 ml of concentrated sulfuric acid in 150 ml of water. The reaction mixture was kept on a boiling water bath for ten minutes from the instant of complete solution of the precipitate, after which it was cooled to room temperature. The colorless crystalline precipitate was filtered off, washed thoroughly with water until no longer acid to Congo red and dried at 50-60°. The yield of diaminouracil sulfate was 11.9 g (70%).

**Preparation of 4-amino-5-formylaminouracil (III). a) From 4,5-diaminouracil sulfate.** A mixture of 24 g of diaminouracil sulfate, 8 g of sodium formate, 3.5 ml of 85% formic acid and 168 ml of water was refluxed for one hour in a flask provided with a reflux condenser and a stirrer. The resulting precipitate was filtered off after cooling to room temperature and was thoroughly washed with water. The yield of the dry formyl derivative was 19.2 g (93.4%).

**b) From 4,5-diacetylaminouracil.** Into a three-necked flask of 500 ml capacity, provided with a stirrer, a thermometer and a reflux condenser, there was placed 114 ml of 10 N sodium hydroxide which was then heated on a boiling water bath to 93-95°. At this temperature there was added 30 g of the diacetyl derivative of 4,5-diaminouracil and the resulting solution was heated on the boiling water bath for two hours. After this period there was added 66 ml of water, the flask contents were cooled to 40° and treated rapidly with 79.5 ml of 85% formic acid. The resulting mixture was refluxed for one hour with continuous stirring after which it was allowed to cool gradually to room temperature over 2-3 hours. The resulting precipitate of 4-amino-5-formylaminouracil was filtered off, washed thoroughly with water and dried at 60-70°. The yield was 18.8 g (79.5%).

It is possible to acidify the reaction mixture after hydrolysis with concentrated hydrochloric acid instead of formic acid. In this case the neutralization is made to acid reaction to Congo red (about 114 ml) at 5-10°. The excess acidity is removed with 10 N sodium hydroxide (about 2.4 ml) until neutral to Congo red. Then there was added to the reaction mixture 14 ml of 10 N sodium hydroxide and 15 ml of 85% formic acid and the formylation process is carried out as in the case with neutralization by means of formic acid.

**Preparation of theophylline (V) and caffeine (VI).** Methylation of the formyl derivative of 4,5-diaminouracil with dimethyl sulfate and the cyclization of the resulting 1,3-dimethyl-4-amino-5-formylaminouracil into theophylline and caffeine were performed under the conditions described for the synthesis of theophylline from urea and sodium cyanoacetate [22]. From 18.8 g of the formyl derivative of 4,5-diaminouracil there was obtained 12.5 g of theophylline (67%). M.p. 268-270° (literature data: m.p. 269° [14]).

Found %: N 31.14, 31.22. $C_7H_8O_2N_4$. Calculated %: N 31.09.

From 12.6 g of theophylline there was obtained 12.7 g of caffeine with m.p. 232-235° (literature data: m.p. 234-236° [23]).

## SUMMARY

1. There was described a method of preparation of theophylline and caffeine from uric acid utilizing as an intermediate product 4,5-diacetylaminouracil.

2. The conditions of preparation of the following intermediate products of the synthesis of theophylline and caffeine are given: 4,5-diacetylaminouracil (II), 4-amino-5-acetylaminouracil (VII), 4,5-diaminouracil sulfate (VIII) and 4-amino-5-formylaminouracil (III).

## LITERATURE CITED

[1] German Patent 121,224; Centralblatt 1901, II, 71.

[2] German Patent 128,212; Centralblatt 1902, I, 549.

[3] German Patent 146,714; Centralblatt 1903, II, 1484.

[4] German Patent 146,715; Centralblatt 1903, II, 1485.

[5] German Patent 151,133; Centralblatt 1904, I, 1430.

[6] E. Fischer and L. Ach, Ber. 30, 2208 (1897).

[7] E. Fischer, Ber. 30, 2220 (1897).

[8] E. Fischer, Ber. 30, 2226 (1897).

[9] German Patent 145,880; Centralblatt 1903, II, 1036.

[10] German Patent 153,122; Centralblatt, 1904, II, 626.

[11] E. Fischer and F. Ach. Ber. 39, 423 (1906).

[12] H. Bredereck, H. G. Schuh and A. Martini, Ber. 83, 201 (1950).

[13] H. Bredereck, J. Hennig and W. Pfleiderer, Ber. 86, 321 (1953).

[14] H. Bredereck, J. Hennig, W. Pfleiderer and G. Weber, Ber. 86, 333 (1953).

[15] I. T. Strukov and L. S. Diskina, Pharmacy (USSR)6, 16 (1945).

[16] E. S. Golovchinskaia, J. Applied Chem. (USSR) 19, 1173 (1946).

[17] V. I. Khmelevskii, Author's certificate 102,848 (1956).*

[18] E. S. Golovchinskaia, J. Gen. Chem. 24, 136 (1954).**

[19] German Patent 144,761; Centralblatt 1903, II, 859.

[20] V. I. Khmelevskii and A. S. Arkhipova, Author's application 2440 (1956).*

[21] German Patent 138,444; Centralblatt 1903, I, 370.

[22] V. I. Khmelevskii and E. I. Abramova, J. Gen. Chem. 28, 1971 (1958).**

[23] E. Fischer and O. Bromberg, Ber. 30, 221 (1897).

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Institute

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*In Russian.

**Original Russian pagination. See C. B. Translation.

# A STUDY IN THE FIELD OF POLYCYCLIC QUINONES

## III. REACTION OF 1-HALOANTHRAQUINONE WITH SECONDARY ALKAROMATIC AMINES

N. S. Dokunikhin and T. N. Kurdiumova

It is known that the halogen atom in $\alpha$-halo substituted derivatives of anthraquinone is replaced relatively readily by residues of primary aliphatic or aromatic amines [1]. The secondary aliphatic amines react with 1-haloanthraquinone under approximately the same conditions as do the primary amines [2]. Diphenylamine does not react with 1-chloroanthraquinone, but does so with 1-iodo- and 1-bromoanthraquinones at a temperature above 200°, forming 1-N,N-diphenylaminoanthraquinone [3]. We failed to find in the literature any data on the reaction of 1-halo substituted anthraquinones with secondary alkaromatic amines and on the description of properties of N,N-alkylaryl substituted 1-aminoanthraquinones.

We showed in preliminary experiments that 1-chloroanthraquinone does not react with methylaniline under the usual conditions of preparation of arylamino derivatives of anthraquinone, i.e., in boiling butanol in the presence of copper catalyst and a basic reagent [4]. Over 95% of the original 1-chloroanthraquinone was isolated from the reaction mixture. However, after heating 1-chloroanthraquinone in excess methylaniline to 170-175° for 7 hours in the presence of potassium acetate and copper acetate and metallic copper there was isolated from the reaction products some 47.8% of 1-N,N-methylphenylaminoanthraquinone, 11% of 1-anilinoanthraquinone and 28.8% of anthraquinone. With ethylaniline under these conditions there was obtained 1.0% of 1-N,N-ethylphenylaminoanthraquinone, 30.8% of anilinoanthraquinone and 55.5% of anthraquinone.

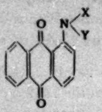
The formation of anthraquinone as the result of heating 1-chloroanthraquinone in nitrobenzene with potassium acetate and copper compounds had been observed in 1912 by Ullmann and Minajeff [5] and later by Bradley [6]. A recent study [7] has been devoted to the dehalogenation of 1-chloroanthraquinone under similar conditions, in which there were examined the effects of temperature, the nature of the solvent and of the acid-binding reagent on the degree of conversion and on the composition of the reaction products. According to these data the replacement of potassium acetate by potassium carbonate leads to a considerable decrease of the rate of dehalogenation and the reaction product is not anthraquinone but 1,1'-dianthraquinonyl. According to our observations, the reaction of 1-chloroanthraquinone with methylaniline is also retarded by the presence of potassium carbonate. As the result of heating 1-chloroanthraquinone with excess methylaniline at 190° for 15 hours in the presence of potassium carbonate and metallic copper, there was isolated 33.5% of unreacted 1-chloroanthraquinone. After 30 hours of heating there was found among the reaction products: 26.7% of 1-N,N-methylphenylaminoanthraquinone, 10.6% of 1-anilinoanthraquinone and 51.5% of unpigmented substance which was free of halogen and which did not melt at 420°. This substance gave an intensely green color with concentrated sulfuric acid, while with metallic opper it gave the characteristic qualitative test for 1,1'-dianthraquinonyl [6]. However, contrary to the data [7], the character of the product of dehalogenation does not depend only on the selection of the acid-binding reagent. In the reaction of 1-bromoanthraquinone with N,N-dicyclohexylamine, with potassium carbonate and copper, there was isolated 37.5% of anthraquinone which did not contain even traces of 1,1'-dianthraquinonyl.

Considering the closeness of the natures of aniline and methylaniline as solvents, it was interesting to compare under the same conditions the degrees of dehalogenation of 1-chloroanthraquinone in its reaction with primary and secondary amines. It turned out that from the reaction products of 1-chloroanthraquinone with aniline it is possible to isolate, along with anilinoanthraquinone, only 1.5% of anthraquinone, which fact is evidently explained by the considerably greater rate of the competing reaction of arylamination by the primary amine. One may expect that owing to the greater mobility of the bromine atom one might reach a higher yield of 1-N,N-methylphenylaminoanthraquinone by starting with 1-bromoanthraquinone. However, in this case the rate of dehalogenation rises to an even greater degree. There was isolated from the reaction mixture some 68% of anthraquinone.

Dealkylation in the reaction of 1-chloroanthraquinone with secondary aliphatic amines (except for dimethylamine) was recently observed by Bradley [8]. In our experiments during the reaction of chloroanthraquinone with N-alkylanilines there also took place the cleavage of the methyl group. As indicated above, the yield of 1-anilinoanthraquinone comprises some 11% in the case of reaction with methylaniline, and some 30.8% – with ethylaniline. The formation of 1-anilinoanthraquinone cannot be explained by a cleavage of the alkyl residue from 1-N,N-alkylphenylaminoanthraquinone. Under the conditions of the reaction (in the presence of potassium acetate, excess methylaniline, metallic copper and its salts) only traces of 1-anilinoanthraquinone were formed from 1-N,N-methylphenylaminoanthraquinone in 8 hours of heating at 175°. One may suppose that the anilinoanthraquinone is formed from the primary amine which forms in the reaction mixture as the result of disproportionation of alkylaniline with simultaneous formation of dialkylaniline. This supposition is confirmed by the fact that in the reaction of 1-chloroanthraquinone with ethylaniline (taken in amount equal to 140% of theoretical) in the presence of a large amount of diethylaniline the yield of anilinoanthraquinone was but 3.5 instead of 30.8% obtained with a large excess of ethylaniline.

1-N,N-Alkylphenylamino derivatives of anthraquinone are readily crystallizing substances which are soluble a majority of organic solvents. They differ from 1-anilinoanthraquinone by the deeper purple color of solutions and by smaller mobility and deeper color of the absorptional layer in chromatographic separation on aluminum oxide. In the following table there are given the data which characterize the absorption of light by carbon tetrachloride solutions of N-alkyl, N-aryl-, N,N-diaryl- and 1-N,N-alkylphenylaminoanthraquinones. 1-N,N-Diphenylaminoanthraquinone which had not been characterized sufficiently well in the literature [3], was synthesized by us from diphenylamine and 1-bromoanthraquinone in the presence of potassium carbonate and metallic copper. In its properties it is very close to the above described N,N-alkylaryl substituted derivatives.

Light Absorption by Solutions in $CCl_4$ of Compounds of General Formula:



| Substituents | | $\lambda'_{max}$ (mμ) | ε' | $\lambda''_{max}$ (mμ) | ε'' | $\lambda'''_{max}$ (mμ) | ε''' |
|---|---|---|---|---|---|---|---|
| X | Y | | | | | | |
| H | $CH_3$ | 315 | 5620 | — | — | 495 | 6850 |
| $CH_3$ | $CH_3$ | 319 | 5770 | 388.5<br>409 | 1450<br>1540 | 495.5 | 4940 |
| H | $C_6H_5$ | 320.5 | 8750 | — | — | 502.5 | 7300 |
| $CH_3$ | $C_6H_5$ | 320 | 5800 | 372 | 3450 | 532 | 2550 |
| $C_2H_5$ | $C_6H_5$ | 320 | 5920 | 372 | 2840 | 537.5 | 1970 |
| $C_6H_5$ | $C_6H_5$ | 320 | 8760 | 380 | 4970 | 535.5 | 2860 |

A comparison of the data from the measurements of light absorption shows that the replacement of hydrogen at the nitrogen atom by alkyl or aryl residue in 1-anilinoanthraquinone causes a shift of the principal absorption maximum by 30-35 m toward the longer wave part of the spectrum. Simultaneously, the intensity of absorption in the visible region drops sharply, which fact is often observed in noncoplanar molecules. The characteristic of light absorption by secondary and tertiary amines is the presence of an additional absorption band in the region of 370-380 m found among the tertiary amines.

## EXPERIMENTAL

**Monoalkylanilines.** Both methyl- and ethylanilines were treated with phthalic anhydride prior to distillation in order to remove the admixture of primary amine (according to B. A. Porai-Koshits [9]). The content of monomethylaniline was 100% and that of monoethylaniline was 93.25% in the distilled amines. The latter product contained 6.5% of diethylaniline.

**1-N,N-Methylphenylaminoanthraquinone.** 1-Chloroanthraquinone (12.1 g) was heated with 40 ml of methylaniline, 5.5 g of potassium acetate, 0.12 g of powdered metallic copper and 0.12 g of copper acetate for seven hours at reflux with good stirring. The color of the reaction mixture changed from yellow to raspberry. The precipitate (I) which formed on cooling was filtered off, washed with methyl alcohol, dilute hydrochloric acid and water, and was then dried. From the resulting lightly colored precipitate (3.65 g) there was isolated by solution in concentrated sulfuric acid with subsequent dilution of the solution to the concentration of 82%, 3 g (28.8%) of anthquinone with m.p. 278-280°. The latter was identified by the absence of depression in mixed melting point with an authentic sample. By further dilution of the sulfuric acid solution there was isolated 0.53 g of deep red substance in which there was established, by chromatographic analysis on aluminum oxide, the presence of 10% of 1-methylphenylaminoanthraquinone and 20% of 1-anilinoanthraquinone.

The liquid remaining after the separation of precipitate (I), with the methyl alcohol used for washing the precipitate (I), was poured into dilute hydrochloric acid with energetic stirring and external cooling. The resulting precipitate (II) was filtered off, washed with dilute hydrochloric acid and water, and was dried. The yield of crude product was 9.73 g. Precipitate (II) was dissolved in carbon tetrachloride. By chromatographic analysis of this solution there was shown the presence in it of 1-anilinoanthraquinone (15.8%) and 1-methylphenylaminoanthraquinone (76.9%). Thus the total yield of 1-N,N-methylphenylaminoanthraquinone was 7.5 g (49.8%) and that of 1-anilinoanthraquinone was 1.64 g (11%). 1-Anilinoanthraquinone isolated by chromatography had m.p. 139-141°. It was identified by the absence of depression in mixed melting point with an authentic sample of 1-anilinoanthraquinone and by the coincidence of the absorption curves for both samples in carbon tetrachloride solution. 1-N,N-Methylphenylaminoanthraquinone had m.p. 130-131° (from alcohol).

Found %: C 80.23, 80.07; H 5.00, 4.82; N 4.28, 4.35. $C_{21}H_{15}O_2N$. Calculated %: C 80.52; H 4.75; N 4.47.

**1-N,N-Ethylphenylaminoanthraquinone.** A mixture of 12.1 g of 1-chloroanthraquinone, 40 ml of ethylaniline, 5.5 g of potassium acetate, 0.42 g of metallic copper and 0.12 g of copper acetate was heated under reflux with good stirring for 7 hours at 170-175°. By filtration of the reaction mixture after cooling and subsequent treatment described above, there was isolated 5.68 g (54.5%) of anthraquinone with m.p. 278-280°. By means of chromatographic analysis there was found in the mixture 0.1 g (0.6%) of 1-N,N-ethylphenylaminoanthraquinone with m.p. 140-143° (from alcohol) and 4.6 g (30.8%) of 1-anilinoanthraquinone.

Found %: C 80.07, 79.86; H 5.20, 5.07; N 4.64, 4.78. $C_{22}H_{17}O_2N$. Calculated %: C 80.73; H 5.20; N 4.28.

**Isolation of anthraquinone from a mixture with 1-anilino- and 1-N,N-methylphenylaminoanthraquinone.** A sample of 4 g of dry product, prepared by filtration of the reaction mixture with a subsequent washing with alcohol and dilute hydrochloric acid, was dissolved in 50 g of 94% sulfuric acid with stirring. To the resulting solution there was added over 1.5 hours with stirring enough dilute sulfuric acid (48.50%) to gradually lower the concentration of the solution to 82%. During this all the anthraquinone precipitated in the form of the sulfate (colorless needles). The mixture was allowed to stand for several hours for completion of crystallization, after which it was filtered through a porous glass filter, washed with 5-10 ml of 82% sulfuric acid, and the precipitate was pressed well on the filter and then was transferred with the aid of a large volume of water into a beaker. The resulting somewhat gray anthraquinone was filtered quantitatively, dried and weighed.

The sulfuric acid solution (acid concentration 82%) was poured into a large volume of water and the precipitated dark red mixture of 1-anilino- and 1-N,N-alkylphenylaminoanthraquinone was filtered off. The mixture may be separated by the chromatographic method. From an artificial mixture of 2 g of anthraquinone and 2 g of 1-anilinoanthraquinone it was possible to remove by this method 1.96 g of anthraquinone (i.e., 98% of initial amount) with m.p. 278-280° and 1.87 g of 1-anilinoanthraquinone with m.p. 132-134.5°.

**Chromatographic isolation of 1-anilino- and 1-N,N-alkylphenylaminoanthraquinones.** A sample of 0.4-0.5 g of the mixture of substances obtained by the separation of excess amine (precipitate (II)) was dissolved in 25-30 ml of carbon tetrachloride. The solution was poured into a column filled with anhydrous aluminum oxide. The chromatogram was developed by the same solvent. The mixture separated into a poorly mobile yellow zone and two more mobile zones (violet and red) which gradually separated from each other. From the separately collected violet-red solution of 1-alkylanilinoanthraquinone and red solution of 1-anilinoanthraquinone the solvent was distilled and the dry residues were weighed. The melting point was determined usually after recrystallization of the residue from alcohol.

1-N,N-Diphenylaminoanthraquinone. A mixture of 1-bromoanthraquinone (5.74 g), diphenylamine (5.1 g), $\alpha$-chloronaphthalene (30 ml), potassium carbonate (3.28 g) and metallic copper (0.1 g) was stirred for 17 hours at 220°. The precipitate which formed on cooling was filtered off, washed with alcohol and water until neutral, and then dried. There was isolated 1.33 g of light gray product which did not melt at 410° and gave an intense green color with concentrated sulfuric acid and metallic copper, which is characteristic of 1,1-dianthraquinonyl. $\alpha$-Chloronaphthalene and excess diphenylamine were steam distilled from the filtrate. By fractional recrystallization from ethyl alcohol there was isolated 2.48 g of the product, which gave brown-red prisms which appeared to be purple in transmitted light; m.p. 181-183°.

Found %: C 82.70, 82.74; H 4.61, 4.55; N 3.66, 3.61. $C_{26}H_{17}O_2N$. Calculated %: C 83.20; H 4.53; N 3.73.

## SUMMARY

1. The reaction of N-alkylanilines with $\alpha$-haloanthraquinones was studied. It was established that as the result of the reaction there are formed N-monoaryl substituted derivatives and the products of dehalogenation of 1-haloanthraquinone, in addition to N,N-alkylarylamino substituted anthraquinone.

2. 1-N,N-Methylphenyl-, 1-N,N-ethylphenyl- and 1-N,N-diphenylaminoanthraquinones were synthesized; their properties were described and the light absorption by the solutions of these substances in carbon tetrachloride was measured.

## LITERATURE CITED

[1] J. Houben, Anthracen and Anthrachinon, Leipzig, 423 (1929).

[2] German Patent 136,777; Friedlander, 6, 374.

[3] E. Laube, Ber. 40, 3565 (1907).

[4] U. S. Patent 2,210,517.

[5] F. Ullmann and W. Minajeff, Ber. 45, 689 (1912).

[6] W. Bradley, J. Chem. Soc. 1951, 2147.

[7] N. I. Artem'ev and A. E. Kretov, J. Applied Chem. (USSR) 26, 1276 (1953).*

[8] W. Bradley and R. F. Maisey, J. Chem. Soc. 1954, 247.

[9] B. A. Porai-Koshits, Aniline Dye Industry (USSR) 4, 295 (1934).

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Organic Intermediates
and Dyes

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* Original Russian pagination. See C. B. Translation.

## STEROIDS

# I. PREPARATION OF 21-BROMOPREGNANOL-17α-TRIONE-3,11,20 FROM PREGNANOL-3β-DIONE-11,20

**O. K. Nikiforova and N. N. Suvorov**

In the synthesis of cortisone acetate from 11α-hydroxyprogesterone [1] by the methods of Djerassi-Gallaher [2-4] as well as by the method developed in our laboratory [5], the reactive oxo group in 3-position of pregnantrione-3,11,20 is selectively reduced with sodium borohydride with formation of pregnanol-3α-dione-11,20. The resulting substance was subjected to further transformations for the introduction of hydroxy groups in positions 17 and 21. Pregnanediol-3α,17α-dione-11,20 was synthesized through the dienol acetate and the monooxide. By bromination of pregnanediol-3α,17α-dione-11,20 Gallaher and co-workers obtained the corresponding 21-bromo derivative. Hydrolysis of 21-bromopregnanediol-3α,17α-dione-11,20 led to pregnanetriol-3α,17α,21-dione-11,20. Oxidation of the secondary hydroxyl in 3-position gave pregnanediol-17α,21-trione-3,11,20 (dihydrocortisone).

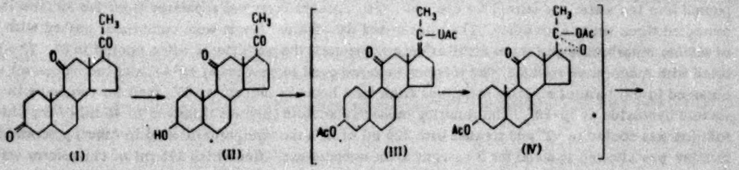
In contrast to the above scheme, in the method from our laboratory, pregnanediol-3α,17α-dione-11,20 was transformed by consecutive or simultaneous bromination and oxidation into 21-bromopregnanol-17α-trione-3,11,20; the replacement of bromine in 21-position by an acetoxy group led to the acetate of dihydrocortisone.

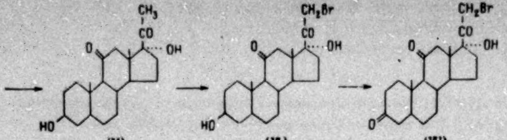
There is an indication in the patent literature [6] that the selective reduction of pregnanetrione over Raney nickel yields not pregnanol-3α-dione-11,20 but its epimer – pregnanol-3β-dione-11,20.

In another patent [7] there is given the most general scheme for transformation of the acetate of pregnanol-3β-dione-11,20 into pregnanediol-3β,17α-dione-11,20 (the constants of this are not cited).

The possibility of construction of a dihydroxyacetone side chain, starting with pregnanol-3β-dione-11,20, is evidently of considerable interest since it opens the possibility to replace the expensive and difficultly obtainable sodium borohydride and to raise the yield of the product considerably in the reduction (96% with nickel instead of 70-72% with sodium borohydride), which facts are very material in the preparation of such an expensive preparation as cortisone, whose synthesis passes through a whole series of steps.

We conducted a synthesis of 21-bromopregnanol-17α-trione-3,11,20 (VII) from pregnanetrione-3,11,20 by the following scheme:





(V) (VI) (VII)

In contrast to the patent data [7], the enolization of (II) was done by us in the medium of acetic anhydride and toluene; we used sulfosalicylic acid for the enolizing reagent [8]. The resulting monoenol acetate (III) was transformed into the oxide (IV) by oxidation with monoperphthalic acid instead of peracetic acid. For hydrolysis of oxide (IV) and preparation of (V) there was used an aqueous methanolic solution of sodium hydroxide. Compounds (III) and (IV) were not isolated in the pure state in the process of this synthesis.

The 21-bromo derivative (VI) was obtained in good yield by bromination of (V) with dioxane dibromide in methanolic medium and the product was smoothly oxidized to (VII) by the action of N-bromosuccinimide.

We consider it a pleasant duty to express our deep gratitude to Iu. N. Sheinker for the spectroscopic studies on the substances prepared by us.

## EXPERIMENTAL

**Pregnanol-3β-dione-11,20 (II).** Into an autoclave made of stainless steel there was placed a solution of 17.2 g of pregnanetrione-3,11,20 (I) in 330 ml of anhydrous methanol and 16.5 g of Raney nickel type W-4. Hydrogenation was run with initial hydrogen pressure of 4 atmospheres for four hours. The reaction product was filtered from the catalyst, the latter was washed on the filter with 30 ml of methanol, the wash liquid was combined with the main filtrate and the methanol was distilled off in vacuo to dryness. To the residue there was added 75 ml of dry ether. A colorless finely crystalline precipitate formed on rubbing. This was filtered off after cooling for two hours in a mixture of ice-salt (−10°); the precipitate was washed with 7 ml of cold ether and dried in vacuum at 40-45°. To the ethereal mother liquor there was added 5 ml of n-heptane. Thereby there was isolated an additional 1 g of the product. After reprecipitation from ether the yield was 0.52 g. The total yield of pregnanol-3β-dione-11,20 was 16.72 g (96.5%); $[\alpha]^{24}D$ + 96° (c 1; $CHCl_3$). The acetate of pregnanol-3β-dione-11,20 has m.p. 163-164°; $[\alpha]^{24}D$ + 98.2° (c 1; $CHCl_3$).

In the infrared spectrum of pregnanol-3β-dione-11,20 in the region of 1350-3500 $cm^{-1}$ there are the following absorption bands: 3403, 2940, 1700, 1456 and 1392 $cm^{-1}$.

**Pregnanediol-3β,17α-dione-11,20 (V).** Ten g of pregnanol-3β-dione-11,20 (II) was dissolved in 50 ml of acetic anhydride and refluxed for 40 minutes. The acetic anhydride was distilled completely in vacuum at bath temperature of 60°. The weight of the acetate was 11.2 g. Into a flask, provided with a fractionating column, a distilling condenser and a thermometer, there was placed 20 ml of acetic anhydride, 188 ml of dry toluene and 0.5 g of sulfosalicyclic acid. The apparatus was dried by distilling over two hours some 15 ml of a mixture of acetic acid, acetic anhydride and toluene. Then to the flask contents there was added a solution of 11.2 g of pregnanol-3β-dione-11,20 acetate in 80 ml of a mixture of toluene and acetic anhydride (prepared from 188 ml of toluene and 20 ml of the anhydride) and, over 12 hours, there was slowly distilled 128 ml of a mixture of acetic acid, anhydride and toluene, while 128 ml of a fresh mixture of toluene with acetic anhydride was being added to the reaction mixture at a rate comparable to that of the distillation. The reaction product was cooled to 1°, poured into ice water and stirred for one hour. The aqueous layer was separated from the toluene layer and extracted three times with ether. The toluene and the ethereal layers were combined, washed with 10% solution of sodium bicarbonate and water, until it became neutral, the wash liquid being cooled to 0°. The product was dried with magnesium sulfate. The solvents were removed in vacuum at 40-45° and the monoenol acetate, obtained in the form of a glassy mass, was dried for 4 hours in vacuum at 60°, then for two hours in vacuum over sodium hydroxide at 70-80°. The resulting monoenol acetate (III) was dissolved in 45 ml of dry chloroform, the solution was cooled to −2° and treated with 120 ml of 21% monoperphthalic acid in ether, precooled to −10°. The mixture was allowed to stand for 3 hours at room temperature, after which 115 ml of chloroform was added and the mixture was washed with cooled 2% sodium hydroxide solution until all the precipitated phthalic acid had dissolved.

The chloroform layer was separated, washed with water and dried with magnesium sulfate. The solvent was removed completely in vacuum. The resulting monooxide (IV) was dissolved in 950 ml of methanol and to the solution was added 22 g of sodium hydroxide in 700 ml of water. The reaction mixture was kept one hour at room temperature, neutralized with 1 : 4 hydrochloric acid and extracted with chloroform. The solution of pregnanediol-3β,17α-dione-11,20 in chloroform was washed with water, dried with magnesium sulfate and freed of the solvent in vacuum at 40°. To the residue there was added 40 ml of dry methylene chloride and the mixture was kept for one day at 2°. The resulting precipitate was filtered off, washed with cooled ether and dried in vacuum at 50°. There was obtained 7.68 g of product with m.p. 209-212°. The mother liquor was shaken for 1.5 hours with activated charcoal, the latter was filtered off, washed with 10 ml of methylene chloride, and the solvent was removed from the filtrate until approximately 30% of the original volume remained. The concentrated solution was kept for three days at 2°. In this manner there was obtained additionally 0.53 g of product with m.p. 206-208.5°. After two recrystallizations from benzene there was obtained 6.5 g of pregnanediol-3β, 17α-dione-11,20 (V) (62% calculated on the initial pregnanol-3β-dione-11,20). It formed snow white shiny plates with m.p. 220-222°; $[\alpha]^{20}D$ +35.13° (c 1; $CHCl_3$).

Found %: C 72.35, 72.42; H 9.05, 8.95. $C_{21}H_{32}O_4$. Calculated %: C 72.41; H 9.19.

In the infrared spectrum of pregnanediol-3β,17α-dione-11,20 in the region of 1350-3500 $cm^{-1}$ there are found the following absorption bands: 3450, 3350, 2940, 1700 and 1456 $cm^{-1}$.

21-Bromopregnanediol-3β,17α-dione-11,20 (VI). Pregnanediol-3β,17α-dione-11,20 (5.53 g) was dissolved in 170 ml of methanol and to this solution there was added dropwise over 4.5 hours 3.94 g of dioxane dibromide in 15 ml of methanol. After completion of the bromination, the colorless solution was rapidly poured into 2.2 liters of water cooled to 1°. The mixture was stirred for one hour, the resulting white precipitate was filtered off, washed with water and dried in vacuum at room temperature over sulfuric acid. Its weight was 6.44 g; m.p. 216-217°. After two recrystallizations from butyl acetate there was obtained 3.88 g of product with m.p. 227.5-228° (with decomposition). The mother liquor was concentrated in vacuum and 1.6 g of additional product was obtained from it. After recrystallization there was obtained 1.12 g of product with m.p. 227.5-227.7°. The total yield of 21-bromopregnanediol-3β,17α-dione-11,20 was 5 g (73%); $[\alpha]^{20}D$ + 70.0° (c 1; acetone).

Found %: C 59.73, 59.84; H 7.34, 7.45; Br 18.27, 18.39. $C_{21}H_{31}O_4Br$. Calculated %: C 59.70; H 7.32; Br 18.72.

21-Bromopregnanol-17α-trione-3,11,20 (VII). To 3.8 g of 21-bromopregnanediol-3β,17α-dione-11,20 there was added 130 ml of methanol, 11.5 ml of water and 3.5 g of N-bromosuccinimide. The mixture was stirred in the dark for one day at room temperature. The precipitated crystals were filtered off, washed with cold methanol and dried in a vacuum desiccator over sulfuric acid. Its weight was 2.88 g. The brightly colored methanolic mother liquor was added dropwise to 1% solution of sodium bisulfite cooled to 0°. The resulting colorless precipitate was filtered off, washed with water until neutral and dried over sulfuric acid. After recrystallization from ethylene chloride there was obtained 0.5 g of the product. Both products were combined and recrystallized from ethylene chloride. The yield was 3.02 g (81.6%); m.p. 215-215.5° (with decomposition); $[\alpha]^{20}D$ +77° (c 1; $CHCl_3$). The mixed melting point of this sample with a sample of 21-bromopregnanol-17α-trione-3,11,20, obtained previously from 21-bromopregnanediol-3α,17α-dione-11,20 showed no depression.

## SUMMARY

1. Starting with pregnanol-3β-dione-11,20 there was accomplished the synthesis of 21-bromopregnanol-17α-trione-3,11,20 – an important intermediate in the previously developed scheme for the synthesis of cortisone acetate.

2. A method of hydrogenation was developed for pregnanetrione-3,11,20 to yield pregnanol-3β-dione-11,20 over Raney nickel catalyst of W-4 type at initial hydrogen pressure of 4 atmospheres.

3. Pregnanediol-3β,17α-dione-11,20 and 21-bromopregnanediol-3β,17α-dione-11,20 were prepared and characterized.

## LITERATURE CITED

[1] D. Peterson, H. Murray, S. Epstein, L. Reineke, A. Waintraub, P. Meister and H. Leigh, J. Am. Chem. Soc. 74, 5933 (1952).

[2] O. Mancera, H. Ringold, C. Djerassi, G. Rosenkranz, S. Sondheimer, J. Am. Chem. Soc. 75, 1286 (1953).

[3] T. Kritchevsky, D. Garmaise and T. Galagher, J. Am. Chem. Soc. 74, 483 (1952).

[4] N. N. Suvorov, Chemical Science and Industry (USSR) No. 4, 406 (1956).

[5] N. N. Suvorov, Medicinal Industry of USSR, No. 3, 22 (1956).

[6] British Patent 723,189; J. Appl. Chem. 5, 910 (1955).*

[7] U. S. Patent 2,671,095; Chem. Abstr. 49, 2532 (1955).

[8] H. Anderson, E. Carrett, F. Lincoln, Jr. Nathan and J. Hogg, J. Am. Chem. Soc. 76, 743 (1954).

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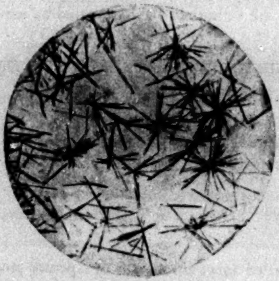
# STEROIDAL SAPOGENINS

## IV. A NEW SARSAPONINE ISOLATED FROM ROOTS OF YUCCA FILAMENTOSA

O. S. Madaeva

In our previous publication [1] it was shown that from the roots of Yucca filamentosa growing on the Black Sea shores of the Caucasus there was isolated about 0.9% of water insoluble saponines which were gradually precipitated after standing in defatted water solutions – extracts of saponines – the precipitates having the appearance of pinkish-brown fine powder. The present work is a continuation of study of these saponins. The colored precipitate was purified by boiling with ether, recrystallization from acetone with charcoal and several recrystallizations from aqueous butanol; finally there was obtained a colorless crystalline precipitate in the form of long needles collected in bundles (see figure). It melted at 283-284° (with decomposition) and according to its composition corresponded to a glucoside of monohydroxysapogenine, containing two molecules of hexose (saponine I). From this there was prepared an acetate [2], the benzene solution of which was passed for purification through a column with aluminum oxide, weakened preliminarily by washing with ethyl acetate. The acetate in its elemental composition was a completely acetylated form of the above mentioned glucoside. After hydrolysis of the acetate with sodium methoxide [3] there was isolated the original saponine.



Crystals of sarsaponine from Yucca filamentosa (magnified 20 times).

After refluxing saponine I with 4 N aqueous methanolic solution of hydrochloric acid there was obtained, as the result of hydrolysis, 57% of a resinous crystalline precipitate. Double chromatography on paper applied to a sample of this precipitate, in the presence of witness-compounds (sarsapogenine and smylagenine) showed that this precipitate consists only of sarsapogenine. The infrared spectrum of the acetate of the sapogenine turned out to be identical with the infrared spectrum of the acetate of sarsapogenine [4].

For clarification of the composition of the carbohydrate residue of the saponine there was examined the composition of the sugars in the aqueous methanolic solution after the acid hydrolysis of saponine and the extraction of the resulting sapogenine with benzene. We used the technique of ascending paper chromatography. The solvent system was that of a mixture of butanol, pyridine and water (3 : 2 : 1.5) [5]; the chromatogram was developed by spraying with 3% solution of p-anisidine in n-butanol containing 3% of hydrochloric acid [6]. After repeated chromatographing with the witness-compounds there were obtained two spots which corresponded in the values of Rf to glucose and galactose, which fact confirmed the data of the elemental analysis.

From the butanol filtrates after recrystallization of saponine I there was isolated a precipitate with a lower decomposition temperature (274-275°); however, its elemental analysis and the study of the aglucone and sugar residue obtained from it showed that it was identical to sarsaponine I.

Sarsaponines of different compositions have been described by various authors in the literature (see Table).

Comparison of Sarsaponines of Various Compositions

| Saponine isolated from | Elemental composition of saponine | M. p. | $[\alpha]_D^{20}$ (in pyridine) | Aglucone | Carbohydrate portion | Lit. ref. |
|---|---|---|---|---|---|---|
| *Sarsaparilla Jamaika* (roots) | $C_{44}H_{78}O_{20} \cdot 7H_2O$ | 248° | —48.5° | Sarsapogenine | Dextrose | [7] |
| *Yucca Schotti* (fruits) | $C_{27}H_{44}O_3(C_6H_{10}O_5)_3$ | 241—245 | | Sarsapogenine | | [8] |
| *Yucca Schidigera* (leaves) | $C_{45}H_{74}O_{18}$ | 265—268 | —48.3 | Sarsapogenine | Glucose, galactose, xylose | [9] |
| | $C_{57}H_{94}O_{28}$ | 293—297 | —46.8 | Sarsapogenine + traces of marcogenine | Five or six molecules of hexose | |
| *Yucca filamentosa* (roots) | $C_{27}H_{44}O_3(C_6H_{10}O_5)_2 \cdot H_2O$ | 283—284 | —41.84 | Sarsapogenine | Hexose, galactose | Present paper |

The sarsaponine isolated by Marker [8] from the fruit of Yucca Schotti and sarsaponines obtained by Wall [9] by enzymic cleavage of natural saponins from the leaves of Yucca Schidigera present the greatest points of interest among these substances; of the latter group, one, as indicated by the author, was contaminated by some marcogenine.

The saponine described by us differs from all those shown in the Table both in composition and in the physical constants; it is a quite individual substance and is a glucoside of sarsapogenine in the composition of which units of glucose and galactose are included.

The infrared spectra were measured by the collaborators of the Physicochemical Laboratory under the direction of Iu. N. Sheinker, for which work I express my gratitude to them.

I express my deep gratitude to L. M. Utkin for the interest shown in this work.

## EXPERIMENTAL

Sarsaponine – glucoside of 5β,25α-spirostan-3β-ol. From the defatted aqueous solutions of saponins prepared from the roots of Yucca filamentosa there precipitated, after distilling off methanol and traces of benzene and standing for several days, some fine pinkish-brown precipitate. This was filtered off, washed with water and ether, and recrystallized from acetone (1 : 200) with charcoal, and then twice from aqueous n-butanol (1 : 50); there was obtained a colorless crystalline substance in the yield of 0.9% based on the root weight. It melted with decomposition at 282-284° (saponine I) after having been dried in a vacuum oven at 100° for five hours; $[\alpha]^{20}D$ −41.84° (c 1; pyridine). It crystallizes with a molecule of water and does not liquefy on exposure to air.

Found %: C 61.82, 62.00; H 8.50, 8.71. $C_{27}H_{44}O_3(C_6H_{10}O_5)_2 \cdot H_2O$. Calculated %: C 61.72; H 8.75.

The substance was dried at 100° and 0.1 mm for six hours.

Found %: C 63.33; H 8.71. $C_{27}H_{44}O_3(C_6H_{10}O_5)_2$. Calculated %: C 63.22; H 8.70.

The anhydrous substance gains in weight extremely rapidly by adding a molecule of water.

From the filtrates after the isolation of saponine I there was obtained a precipitate which after recrystallization from methanol had decomposition point at 274-276° (saponine II); this was dried for 4.5 hours at 100° and 15 mm.

Found %: C 61.63; H 8.60. $C_{27}H_{44}O_3(C_6H_{10}O_5)_2 \cdot H_2O$. Calculated %: C 61.72; H 8.75.

**Sarsaponine acetate.** The saponine (I) (0.3 g) was refluxed for two hours with 1 ml of acetic anhydride in the presence of 1 ml of pyridine. The cooled solution was poured into 10 volumes of water acidified with hydrochloric acid; the resulting somewhat tarry precipitate was extracted with benzene, the benzene solution was washed with water until neutral, dried and shaken with charcoal. After distillation of benzene there remained 0.4 g of a slightly yellowish viscous transparent uncrystallizable mass. For purification this was dissolved in 3 ml of benzene and passed through a column with 1.3 g of aluminum oxide which had been weakened by a preliminary washing with ethyl acetate. Washing with benzene gave 0.34 g of colorless glassy residue which was readily soluble in all organic solvents; on evaporation of such solutions there remained an uncrystallizable film.

Found %: C 61.49, 61.53; H 7.59, 7.68. $C_{53}H_{78}O_{20}$. Calculated %: C 61.48; H 7.59.

**Hydrolysis of saponine acetate.** The saponine acetate (0.25 g) was dissolved in 3.5 ml of anhydrous methanol and to this was added 7 ml of methanolic solution of sodium methoxide prepared from 0.02 g of sodium. The solution became turbid shortly and after one hour there began to form a colorless crystalline precipitate of the saponine. This was filtered off on the following day, washed with 5 ml of cold alcohol acidified with acetic acid, followed by 2 ml of alcohol and ether. After drying in vacuum at 100° there was obtained 0.15 g of the product with m.p. 282-284°; a small precipitate of the saponine also formed in the filtrate.

**Sarsapogenine.** The saponine with m.p. 282-284° (0.3 g) was refluxed in a small flask with 28 ml of 50% methanol and 17 ml of concentrated hydrochloric acid in the presence of 10 ml of benzene for four hours. The aqueous methanolic layer was separated, extracted with benzene and left for the determination of sugars. Sapogenine was isolated from the benzene solutions. After recrystallization from ether it did not give a depression in mixed melting point with a specimen of sarsapogenine (m.p.193-196°), while in mixed melting point with a specimen of smylagenine (m.p. 183-184°) melting began at 177°. The isolated sapogenine corresponded to sarsapogenine in the value of its Rf; the infrared spectrum of the acetate prepared from it under conventional conditions gave a complete coincidence with the infrared spectrum of sarsapogenine acetate [9].

**Determination of composition of sugars.** From the aqueous methanol hydrochloric acid solution the solvents were distilled in vacuum at 45°, methanol being added several times for the complete removal of hydrochloric acid. The determination of sugars in the resulting aqueous solution by means of chromatography on paper gave two spots which in their values of Rf corresponded to galactose and glucose that had been deposited alongside on the paper.

## SUMMARY

From the roots of Yucca filamentosa there was isolated one previously undescribed glucoside of sarsapogenine, containing two molecules of hexose in the sugar portion: glucose and galactose.

## LITERATURE CITED

[1] O. S. Madaeva, J. Gen. Chem. No. 28, 551 (1958).*

[2] E. S. Rothman, M. E. Wall and G. R. Eddy, J. Am. Chem. Soc. 74, 4013 (1952).

[3] E. Fischer and M. Bergmann, Ber. 52, 852 (1919).

[4] C. R. Eddy, M. E. Wall and M. K. Serota, Anal. Chem. 25, 266 (1953).

[5] A. Jeanes, C. S. Wise and R. J. Dimler, Anal. Chem. 23, 415 (1951).

[6] L. Hongh, J. K. N. Jones and W. H. Wadman, J. Chem. Soc. 1950, 1702.

[7] F. B. Power and A. H. Salway, J. Chem. Soc. 105, 201 (1914).

[8] R. E. Marker and J. Lopez, J. Am. Chem. Soc. 69, 2389 (1947).

[9] M. M. Krider, J. R. Branaman, and M. E. Wall, J. Am. Chem. Soc. 77, 1238 (1955).

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# STEROIDAL SAPOGENINES

## V. SAPOGENINES OF LEAVES OF AGAVE AMERICANA L.

N. A. Serova and O. S. Madaeva

In the study of plants of USSR flora in respect to their content of steroidal saponines there is interest not only in new plant species but also in those in which the steroidal sapogenines had been found previously. The effect of climatic conditions, soil and locality, in which the plant is collected, on the nature of the steroidal sapogenines which enter the composition of the saponines of a given plant, had been noted by a number of authors [1, 2]. This was confirmed by the example of roots of Yucca filamentosa growing on the Black Sea coast of Caucasus and in southwestern parts of Carolina. In the roots of the former there were found sarsapogenine, hytogenine and hecogenine [3, 4] while in the latter there was found hytogenine (about 1.1%) [5].

The present work is devoted to the study of the composition of sapogenines of the leaves of Agave americana L., cultivated on the Black Sea coast of the Caucasus. It is known that Marker [6] had isolated from the leaves of this species a hecogenine (0.4%) which was also obtained by French scientists [7] from the leaves of this Agave grown in the south of France.

We ran the extraction of saponines in a Sohxlet apparatus with a mixture of water and butanol (2 : 3). Xylene was used for defatting of the aqueous solutions of saponines and for further extraction of sapogenines after acid hydrolysis and after the alkaline hydrolysis.

Separation of the summary technical sapogenines was accomplished by the method of chromatography on aluminum oxide; the composition of sapogenines in the eluates was determined by means of paper chromatography [8].

As a result of this work there was obtained hecogenine in 0.2% yield and there was shown the presence of rocogenine on the basis of a comparison of the values of Rf of the substance obtained from methanolic eluates (Rf 0.66) with a sample of rocogenine (Rf 0.62) synthesized by us by reduction of hecogenine with sodium borohydride [9]. The infrared spectra of their acetates proved to be similar.

### EXPERIMENTAL

The macerated fibrous mass of dry leaves of Agave (140 g) was extracted in a Sohxlet apparatus with 530 ml of a mixture of butanol and water (3 : 2) over twenty hours. The resulting extract was transferred to a separatory funnel. To the lower aqueous layer (275 ml) there was added 13.75 g of sodium chloride and the solution was adjusted to pH 4-5 with hydrochloric acid. Then the solution was subjected to extraction with saturated aqueous butanol (four times 100 ml each). The wash butanol solutions were added to the main solution and these were washed with 5% solution of sodium chloride at pH 4-5 (1/3 of total volume). To the washed butanol solution of saponines there was added 1/2 volume of water and the butanol was distilled completely in the form of an azeotropic mixture. To the aqueous solution in saponines there was added an equal volume of methyl alcohol, the aqueous alcoholic solution was extracted with xylene (four times) to remove lipoids, after which hydrolysis was run.

The defatted aqueous alcoholic solution of saponines (150 ml), 75 ml of concentrated hydrochloric acid and 150 ml of xylene were refluxed for four hours. After separation in the xylene layer, the aqueous alcoholic layer was subjected to extraction with xylene. The xylene extracts were combined, washed with a saturated solution of sodium chloride and concentrated to the volume of 50 ml. For running the alkaline hydrolysis there was added 30 ml of 10% methanolic solution of potassium hydroxide and the mixture was boiled for one hour. After cooling, the xylene layer was separated while the aqueous alcoholic layer was extracted several times with xylene. The combined xylene extracts were washed with water until neutral. Xylene was distilled from the xylene solution after having been dried with sodium sulfate and there was obtained 2.4 g of summary sapogenines in the form of a dark crystallizing mass. This mass was dissolved in 35 ml of benzene and deposited on the column with 40 g of activated commercial aluminum oxide. Washing with benzene and a mixture of benzene with chloroform (4:1) led to the separation of oily impurities which do not contain sapogenines; tarry crystalline precipitate passes along with chloroform, this material by its Rf value of 0.72 consisting evidently of hecogenine. The residue in the column was eluted with methanol. From the chloroform eluates containing hecogenine, the solvent was removed by distillation and the residue was washed with heptane, then with cold acetone. After recrystallization from ethyl acetate there was obtained the precipitate with m.p. 244-247°. This substance by its elemental composition, specific rotation and m.p. corresponded to hecogenine [3, 4, 6].

2,4-Dinitrophenylhydrazone of hecogenine was obtained by mixing hot saturated alcoholic solutions of hecogenine and 2,4-dinitrophenylhydrazine (1:1) in the presence of hydrochloric acid. The 2,4-dinitrophenylhydrazone of hecogenine formed thin yellow needles from ethyl alcohol; m.p. 244-246° (with decomposition).

Found %: N 9.07. $C_{33}H_{46}O_7N_4$. Calculated %: N 9.2.

Hecogenine acetate was prepared by refluxing hecogenine with three parts of acetic anhydride for thirty minutes. The product was recrystallized from acetone. M.p. 241-243°.

Literature data: 243°, 252° [6]. Its infrared spectrum agreed completely with those described in the literature [10].

The residues of methanolic eluates were an uncrystallizable tarry mass. By means of paper chromatography there were obtained two spots with Rf values of 0.62 and 0.76 (solvent – mixture of iso-octane, chloroform and acetic acid: 100 : 40 : 4). After treatment with Girard T reagent [11] hecogenine was isolated from the ketonic fraction. The resulting spot from a sample taken from the nonketonic fraction had the Rf value of 0.66 (solvent – mixture of iso-octane, chloroform and acetic acid: 100 : 40 : 4). After deposition on paper, the synthetic hecogenine had Rf 0.62.

Acetylation of samples of the nonketonic fraction and of the prepared sample of rocogenine (for infrared spectra) was run under the usual conditions by refluxing with acetic anhydride for 3-4 minutes.

## SUMMARY

1. It was shown that leaves of Agave americana L. cultivated on the Black Sea coast of the Caucasus contain 0.2% of hecogenine with a small admixture of rocogenine.

2. For isolation of sapogenines there was used the method of extraction with aqueous butanol and by defatting with xylene.

## LITERATURE CITED

[1] R. E. Marker, R. B. Wagner, P. R. Ulshafer, E. L. Wittbecker, D. P. J. Goldsmith and C. H. Ruof, J. Am. Chem. Soc. 69, 2221 (1947).

[2] M. E. Wall, M. M. Krider, C. F. Kewson, C. R. Eddy, J. J. Willamon, D. S. Corell and H. S. Gentry, J. Am. Pharm. Ass. 43, 1 (1954).

[3] O. S. Madaeva, J. Gen. Chem. 28, 551 (1958).*

[4] O. S. Madaeva, J. Gen. Chem. 28, 1989 (1958).*

[5] R. E. Marker, R. B. Wagner, P. R. Ulshafer, E. L. Wittbecker, D. P. J. Goldsmith and C. H. Ruof, J. Am. Chem. Soc. 69, 2229 (1947).

[6] R. E. Marker, R. B. Wagner, P. R. Ulshafer, E. L. Wittbecker, D. P. J. Goldsmith and C. H. Ruof, J. Am. Chem. Soc. 65, 1199 (1943).

[7] S. Heitz, H. Lapin, Ch. Sannie and P. Barchewitz, Bull. Soc. Chim. Biol. 36, 227 (1954).

---

*Original Russian pagination. See C. B. Translation.

[8] Ch. Sannie and H. Lapin, Bull. Soc. Chim. 1952, 1083.

[9] R. B. Woodward, F. Sonderheimer and D. Taub, J. Am. Chem. Soc. 73, 3547 (1951).

[10] C. R. Eddy, M. E. Wall and M. K. Scott, Anal. Chem. 25, 266 (1953).

[11] A. Girard and S. G. Sandulesco, Helv. Chim. Acta. 19, 1095 (1936).

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# EFFECT OF SUBSTITUENTS IN THE MOLECULES OF INHIBITORS ON THEIR PROTECTIVE PROPERTIES IN AUTOXIDATION OF α-PINENE

E. N. Novikova

The purpose of this work is the study of the process of autoxidation of α-pinene in the presence of an initiator and antioxidants in connection with the various chemical nature and structure of their molecules.

It is known that α-pinene, as an unsaturated compound, is readily subjected to autoxidation [1], which is accelerated by oxides and salts of metals [2]. The facile oxidizability of α-pinene is also connected with the fact that phenols contained in turpentine are extracted from the latter in the process of purification and fractional distillation and thus α-pinene is deprived of the natural antioxidants. Therefore for the retardation of autoxidation of α-pinene it is necessary to add antioxidants to it.

One might expect that stabilization of α-pinene by inhibitors, just as in the case of cracked gasolines [3], is more advantageous economically than is its purification by a second distillation. The primary products of autoxidation of α-pinene are hydroperoxides [4, 5] which initiate the process of its further oxidation. Termination of this chain reaction of autoxidation may be realized by reaction of antioxidants with the radical of the hydrocarbon undergoing the oxidation or with oxygen [6].

The inhibiting action of antioxidants depends on the chemical nature and structure of their molecules [7, 8]. Therefore for comparative evaluation of the activity of inhibitors and for the approach to the explanation of the mechanism of their action, it was interesting to follow the accumulation of peroxide compounds in α-pinene.

## EXPERIMENTAL

α-Pinene that was used was taken from production, being obtained from dry distillation turpentine; it was twice distilled from metallic sodium; b.p. 155° at 760 mm, $d^{20}_4$ 0.8576, $n^{20}D$ 1.4657.

For retardation of the process of autoxidation of α-pinene, there were added to it: phenols, phenol derivatives, diphenylamine, naphthalene and other compounds, in amounts of 0.01 millimole of antioxidant per one mole of α-pinene. The autoxidation of α-pinene proceeded in air in diffuse daylight. α-Pinene, both pure and that with added antioxidants, was poured in 24 ml lots into wide-necked flasks of 100 ml capacity, which were left open at 18-20° for prolonged periods.

After definite time intervals samples were taken and in these there were determined, by iodometric method [9], the amounts of peroxide compounds that were present. To a sample of the self-oxidizing α-pinene (about 1 g) there was added 15 ml of 98% acetic acid and 5 ml of 20% potassium iodide solution. The mixture was allowed to stand for 15 minutes at 20°, then the separated iodine was titrated with 0.1 N solution of sodium thiosulfate. A blank run was made in parallel. The amount of peroxide compounds was calculated in milliliters of 0.1 N solution of sodium thiosulfate per 100 g of α-pinene.

For titration of 1.0162 g of α-pinene after 30 days of autoxidation there was required 7.95 ml of 0.1 N sodium thiosulfate. For titration of 0.9846 g of α-pinene after 30 days of autoxidation in the presence of hydroquinone there was required 1.6 ml of 0.1 N sodium thiosulfate. In the blank experiment there was consumed 0.1 ml of 0.1 N sodium thiosulfate. Thus, the amount of peroxide compounds in 100 g of the oxidized α-pinene was equal to 772.5 ml of 0.1 N sodium thiosulfate, while per 100 g of α-pinene oxidized with addition of hydroquinone this amount was equal to 152.5 ml of 0.1 N sodium thiosulfate. For titration of 0.0896 g of freshly

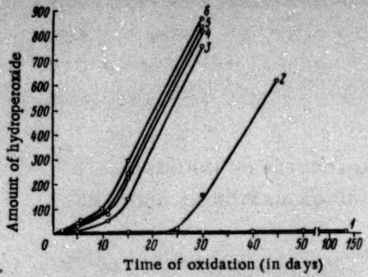

Fig. 1. Effect of phenols and their derivatives on formation of peroxide compounds in α-pinene.
1) Pyrocatechol, pyrogallol, o-aminophenol and p-aminophenol; 2) hydroquinone, 3) thymol, 4) guaiacol and orcin, 5) p-butylphenol and p-cumylphenol, 6) α-pinene without additives.

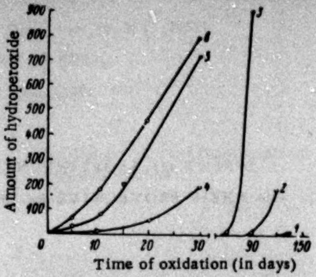

Fig. 2. Effect of derivatives of biphenyl and other compounds on formation of peroxide compounds in α-pinene.
1) p-Aminodiphenylamine, 2,4-diaminodiphenylamine, p-hydroxydiphenylamine and 1,4-diphenylphenylenediamine; 2) diphenylcarbazide; 3) diphenylcarbazone; 4) diphenylamine; 5) phenylsemicarbazide; 6) α-pinene without additives.

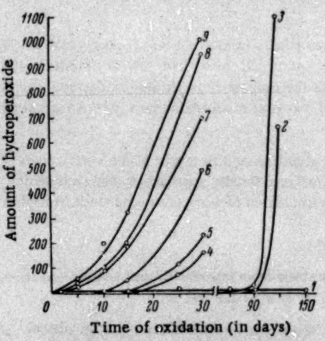

Fig. 3. Effect of derivatives of naphthalene on formation of peroxide compounds in α-pinene.
1) Dinaphthylphenylenediamine; 2) α-naphthol; 3) p-hydroxyneozone D; 4) α-naphtholphthalein; 5) β-naphthol; 6) neozone D; 7) α-naphthylamine; 8) naphthol AS; 9) α-pinene without addends.

distilled α-pinene there was required 0.1 ml of 0.1 N sodium thiosulfate, i.e., peroxide compounds were absent.

Along with the determination of peroxide compounds, the autoxidation of α-pinene was followed by determinations of its index of refraction (with Abbe refractometer) and density. These measurements showed that in α-pinene in the absence of antioxidants (such as pyrocatechol or p-hydroxydiphenylamine) during the induction period of oxidation (Fig. 1-3) the peroxide compounds were not formed in measurable (by titration) amounts. Here the density ($d^{20}_4$ 0.8579) and index of refraction ($n^{20}D$ 1.4659) remained almost the same as in the original α-pinene. Conversely, pure α-pinene, after three months of autoxidation, was characterized by the following constants: $d^{20}_4$ 0.9660, $n^{20}D$ 1.4832, i.e., α-pinene untreated with an antioxidant suffers a deep-seated oxidation.

Experimental data (Fig. 1-6)* show that the various (in their chemical nature) antioxidants inhibit the process of formation of peroxides in α-pinene to different degrees. Phenols (Fig. 1) with hydroxy groups in ortho-position (pyrocatechol and pyrogallol), o- and p-aminophenols, are active inhibitors of the process of formation of peroxide compounds in α-pinene, while the m-isomers (resorcinol and m-aminophenol) do not show the inhibiting action. Replacement of hydrogen in one of the hydroxy groups in the pyrocatechol molecule by a methyl group (guaiacol) sharply lowered the high inhibitory activity of pyrocatechol. The complication of the hydroquinone molecule by replacement of its polar group HO by the group $C(CH_3)_3$ (p-butylphenyl) or by the group $C_6H_5C(CH_3)_2$ (p-cumylphenol) caused a weakening of the antioxidant action.

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*In all graphs the amount of hydroperoxide is expressed in milliliters of 0.1 N solution of sodium thiosulfate per 100 g of α-pinene.

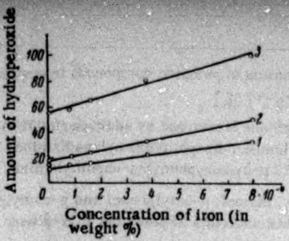

Fig. 4. Effect of iron palmitate on formation of peroxide compounds in α-pinene.
1) After 2 days, 2) after 3 days, 3) after 9 days of autoxidation.

Diphenylamine (Fig. 2) weakly inhibits the formation of peroxides in α-pinene. Introduction of the $NH_2$ group (p-aminodiphenylamine) or the $NHC_6H_5$ group (1,4-diphenylphenylenediamine) into the molecule of diphenylamine leads to a sharp increase of the inhibiting action. In comparing the inhibiting activity and the structural formulas of diphenylcarbazide and diphenylcarbazone one may suppose that the high activity of the former is connected with the presence of four secondary amine groups in its molecule. The relatively smaller activity of diphenylcarbazone is evidently connected with the replacement of two amino groups by an azo group.

In examining the retarding action of naphthalene derivatives (Fig. 3; β-naphthol, β-naphthylamine naphthol AS) it is clear that the nature and the polarity of the substituent groups HO, $NH_2$ and $CONHC_6H_5$ exert their effect on the activity of the inhibitor in the formation of peroxides in α-pinene. The ability of the molecule to donate its mobile hydrogen [10] and thus to retard to a greater or lesser degree the process of autoxidation, and hence the process of formation of peroxides, it is connected with polarity.

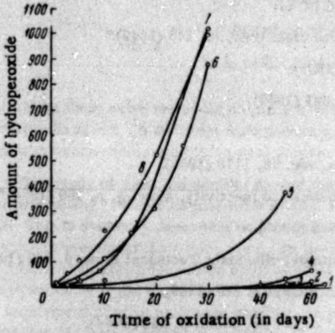

Fig. 5. Effect of antioxidants on formation of peroxide compounds in α-pinene containing iron palmitate.
1) p-Hydroxydiphenylamine, 2) o- and p-aminophenols, 3) 2,4-diaminodiphenylamine, 4) p-aminodiphenylamine, 5) diphenylamine, 6) α-pinene without addends, 7) pyrocatechol, 8) α-pinene with iron palmitate.

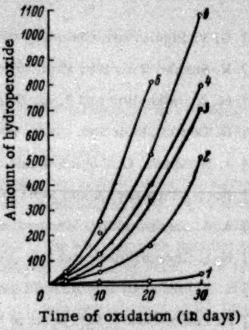

Fig. 6. Effect of derivatives of naphthalene on formation of peroxide compounds in α-pinene containing iron palmitate.
1) p-Hydroxyneozone D, 2) neozone D, 3) β-naphthol, 4) α-pinene without additives, 5) β-naphthylamine, 6) α-pinene with iron palmitate.

In α-pinene during contact with metallic parts of equipment (in the process of its production from turpentine), pipes and tanks, there accumulate compounds of iron which may accelerate autoxidation of α-pinene and our experiments showed (Fig. 4) that an insignificant amount of iron ($0.794 \times 10^{-4}$%) introduced into α-pinene in the form of iron palmitate accelerated the accumulation of peroxides in α-pinene. As to the activity of inhibitors in the presence of iron palmitate (1 mg of iron per 100 ml of α-pinene), the data obtained by us (Figs. 5 and 6) show that the effective inhibitors of accumulation of peroxides in α-pinene are the compounds which contain simultaneously both amino and hydroxy groups: p-hydroxydiphenylamine, o- and p-aminophenols and p-hydroxyphenyl-β-naphthylamine.

## SUMMARY

1. The relative activity of inhibitors on the process of formation of peroxide compounds in α-pinene in diffuse light at 18-20° was studied.

2. It was established that the formation of peroxides in α-pinene is retarded by addition (0.001%) of pyrocatechol, pyrogallol, p- and o-aminophenols, p-hydroxydiphenylamine, dinaphthylphenylenediamine, 1,4-diphenylphenylenediamine, p-aminodiphenylamine, α-naphthol and p-hydroxyphenyl-β-naphthylamine.

3. It was found that derivatives of phenols: guaiacol, orcin, thymol, p-butylphenol and p-cumylphenol (0.01 millimole per 1 mole of α-pinene) are weak inhibitors of accumulation of peroxides in α-pinene.

4. It was shown that the initiating action of iron palmitate on the formation of peroxides exists and the relative activity of o- and p-aminophenols, derivatives of diphenylamine and naphthalene in the presence of iron palmitate was studied.

5. It was shown that the activity of the inhibitor is determined by two factors – polarity of the inhibitor molecule and the mobility of hydrogen connected with the polarity.

## LITERATURE CITED

[1] G. V. Pigulevskii, Chemistry of terpenes, Publ. Leningrad State Univ., p. 145 (1949).*

[2] K. Suzuki, Bull. Inst. Phys. Chem. Res. Japan 14, 179 (1935).

[3] M. N. Mikhailov and B. M. Neiman, J. Gen. Chem. 6, 821 (1936).

[4] G. Dupont, Bull. Soc. Chim. 1948, 838.

[5] R. N. Moore, C. Golumbik and G. Ficher, J. Am. Chem. Soc. 78, 1173 (1956).

[6] N. N. Semenov, About some problems of chemical kinetics and reactivity, Moscow, p. 159 (1954).*

[7] A. S. Kuz'minskii, Progr. Chem. (USSR) 27, 842 (1955).

[8] N. I. Chernozhukov and S. E. Krein, Oxidizability of mineral oils; State Technical Press, p. 202 (1946).*

[9] S. S. Medvedev and A. Pod'iapol'skaia, J. Phys. Chem. (USSR) 13, 719 (1939).

[10] N. F. Ermolenko, Sci. Notes of Belorussian State Univ. No. 20, ser. chem. p. 153 (1954).

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*In Russian.

# LETTERS TO THE EDITOR

## ABOUT PROPERTIES OF POLYAMIDES WITH SILOXANE GROUPINGS

V. V. Korshak, P. M. Frunze, D. N. Andreev and E. V. Kukharskaia

The considerable interest aroused by organosilicon compounds led us to take up a study of the problem of whether or not siloxane groups in the chain of a dicarboxylic acid affect the properties of polyamides incorporating such an acid. For this purpose we prepared polyamides from three dicarboxylic acids of the following structures:

$$HOOC{-}(CH_2)_2{-}Si(R_1R_2){-}O{-}Si(R_1R_2){-}(CH_2)_2{-}COOH,$$

where

$$1)\ R_1 = R_2 = CH_3,\ 2)\ R_1 = R_2 = C_2H_5,\ 3)\ R_1 = CH_3,\ R_2 = C_2H_5.$$

From these acids there was prepared a series of polyamides by polycondensation with various aliphatic and aromatic diamines. In addition, from mixtures of these acids and from mixtures of these acids with adipic acid with hexamethylenediamine there were prepared several series of mixed polyamides.

The study of these polyamides showed that the introduction of the siloxane links leads to the formation of polymers having rubber-like properties as well as lower melting points in comparison with polymers from azelaic acid. This is evidently dependent both on the effect of the siloxane grouping and on the presence of side chain substituents present at the silicon atom. In favor of this explanation there is the circumstance that replacement of the methyl radicals of the silicon atom by ethyl radicals causes a lowering of the melting point. The presence of side substituents is the cause for the hindrance of packing of the chains and of their orderliness. Therefore it is not surprising that after prolonged standing the polyamides prepared by us slowly crystallized, which fact is reflected in the rise of melting point and formation of turbidity, as well as decrease of elasticity.

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# THE PROBLEM OF THERMODYNAMIC STUDY OF LOWER CHLORIDES OF WOLFRAM (TUNGSTEN)

S. A. Shchukarev, G. I. Novikov and N. V. Andreeva

The density of saturated and unsaturated vapor of wolfram pentachloride was measured by the static method with a quartz membrane null manometer. It was shown by the opticо-tensimetric method that gaseous wolfram pentachloride disproportionates forming in the gaseous phase wolfram tetra- and hexachlorides. Direct measurement of molecular weight of the vapor of wolfram pentachloride established the presence in it of up to 10% of dimer $W_2Cl_{10}$.

The densities of disproportionation of wolfram tetra- and di-chlorides were also measured by the static method with a quartz membrane. The results of the measurements showed that the tetrachloride disproportionates with formation, in the gas phase, of wolfram pentachloride, while $WCl_2$ disproportionates with formation of penta- and tetrachlorides of wolfram. From the data on measurement of vapor densities we calculated the thermodynamic characteristics of the process (see table).

| Processes | ΔH (in kilo-calories) | ΔS (in entropy units) | Temperature interval |
|---|---|---|---|
| $[WCl_5]_{sol} = (WCl_5)_{vap}$ | 18.5 ± 0.5 | 33.1 ± 0.7 | 150 — 253°<br>(M. p. 253°) |
| $(WCl_5)_{liq} = (WCl_5)_{vap}$ | 13.6 ± 0.9 | 23.9 ± 0.9 | 253 — 330°<br>(B. p. 288°) |
| $(W_2Cl_{10})_{vap} = 2(WCl_5)_{vap}$ | 7.9 ± 0.7 | 13.9 ± 0.9 | 280 — 450 |
| $2(WCl_5)_{vap} = (WCl_4)_{vap} + (WCl_6)_{vap}$ | ~ 6 | ~-5 | 300 — 500 |
| $3[WCl_4]_{sol} = [WCl_2]_{sol} + 2(WCl_5)_{vap}$ | 66 ± 4 | 90 ± 4 | 300 — 430 |
| $[WCl_2]_{sol} + 2(WCl_5)_{vap} = 3(WCl_4)_{vap}$ | 50 ± 4 | 60 ± 4 | 450 — 600 |
| $2[WCl_2]_{sol} = [W]_{sol} + (WCl_4)_{vap}$ | 59 ± 2 | 67 ± 2 | 490 — 580 |
| $5[WCl_2]_{sol} = 3[W]_{sol} + 2(WCl_5)_{vap}$ | 129 ± 4 | 145 ± 4 | 490 — 580 |

Insofar as the experimentally secured thermodynamic characteristics of the processes carried out above are absent from the literature, while Brewer's data published in this monograph have primarily a calculational character, we may consider that the values obtained by us are evidently more accurate than those accepted in various tables.

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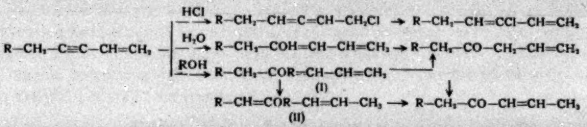
Leningrad State University

# CONCERNING THE ORDER OF ADDITION OF WATER AND ALCOHOLS TO VINYLALKYLACETYLENES

A. A. Petrov and B. S. Kupin

We discovered during a study of reactions of addition to vinylalkylacetylenes that the order of addition of water, alcohols and hydrogen halides to these compounds is not the same. In case of water and alcohols, the hydrogen adds to the second atom of the conjugated system, while in case of hydrogen halides the hydrogen adds to the first atom. Thus in these reactions the atoms of the conjugated system change their polarity.



$$R{-}CH_2{-}C{\equiv}C{-}CH{=}CH_2 \xrightarrow{HCl} R{-}CH_2{-}CH{=}C{=}CH{-}CH_2Cl \rightarrow R{-}CH_2{-}CH{=}CCl{-}CH{=}CH_2$$

$$R{-}CH_2{-}C{\equiv}C{-}CH{=}CH_2 \xrightarrow{H_2O} R{-}CH_2{-}COH{=}CH{-}CH{=}CH_2 \rightarrow R{-}CH_2{-}CO{-}CH_2{-}CH{=}CH_2$$

$$R{-}CH_2{-}C{\equiv}C{-}CH{=}CH_2 \xrightarrow{ROH} \underset{(I)}{R{-}CH_2{-}COR{=}CH{-}CH{=}CH_2} \rightarrow R{-}CH_2{-}CO{-}CH_2{-}CH{=}CH_2$$

$$\underset{(II)}{R{-}CH{=}COR{-}CH{=}CH{-}CH_3} \rightarrow R{-}CH_2{-}CO{-}CH{=}CH{-}CH_3$$

The order of addition of hydrogen halides to vinylalkylacetylenes has been established previously [1, 2].

The structure of ketones formed in hydration of vinylmethyl- and vinylethylacetylenes in the presence of mercuric sulfate was proved by hydrogenation to the corresponding saturated ketones (methyl propyl ketone and ethyl propyl ketone) and by their infrared spectra. The products contained a small admixture of allyl ketones.

The structure of ethers formed as the result of addition of alcohols to vinylmethyl- and vinylethylacetylenes in the presence of potassium hydroxide at 150° was established by their infrared spectra (only the frequencies of 1,3-diene group are present) and by their transformation under the action of dilute sulfuric acid into the corresponding alkyl propenyl ketones, which were then reduced over palladium on calcium carbonate to methyl and ethyl propyl ketones.

The spectral data indicate that along with ethers (I) there are also formed the products of their isomerization – ethers (II).

The nonconcordance of the order of addition of water and alcohols to that of hydrogen halides may be explained, in our opinion, by the differences in the mechanism of addition of these substances and by the ease of redistribution of electron density in molecules of vinylalkylacetylenes (dipole moment of vinylalkylacetylenes is low in comparison with that of vinylacetylene and is equal to about 0.6 D). Both electrophilic addition of a proton and the nucleophilic addition of the OR anion or some complex with participation of water in the Kucherov reaction, begin at the first carbon atom, since only this order of addition leads to the origin of a stable cation or anion with preservation of conjugation. This explanation meets a difficulty in connection with the fact that isoalkenylacetylenes (for example, isopropenylacetylene) also have lowered values of dipole moments but add hydrogen halides, water and alcohols in the same order (this was studied by many authors).

The discovered regularity should have a general explanation, one common for the reactions of addition of water and alcohol to divinylacetylenic hydrocarbons discovered by I. N. Nazarov [3]. We believe that the solution of this problem is of general interest for the theory of reactions of conjugated systems.

## LITERATURE CITED

[1] A. A Petrov and E. A. Leporskaia, J. Gen. Chem. 23, 1471 (1953).*

[2] A. A. Petrov and Iu. I. Porfir'eva, J. Gen. Chem. 27, 2076 (1957).*

[3] I. N. Nazarov, Progr. Chem. 20, 71 (1951).

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# SYNTHESIS OF LEAD TETRAACETATE BY ELECTROCHEMICAL OXIDATION OF LEAD DIACETATE AT THE ANODE

M. Ia. Fioshin and L. I. Kazakova

Lead tetraacetate is a strong oxidizing agent with a wide range of oxidizing action [1]. The chemical method of synthesis of lead tetraacetate consists of treatment of red lead with glacial acetic acid [2]. The method has the drawback that only one third of the lead entering into the make-up of the red lead is utilized, and two thirds goes into the discard as lead diacetate. It is possible to increase the utilization of lead by simultaneous treatment of the red lead with acetic acid and chlorine [3]. However, in this case one third of the lead is lost as chloride, purification from which is a rather difficult operation involving unavoidable losses of lead tetraacetate. The presence of the slightest contamination of the lead tetraacetate with the chloride is undesirable, since chlorination of organic compounds may occur along with oxidation. As a result of all the purification and separation operations the yield of lead tetraacetate totals 40-50%.

Attempts at electrochemical synthesis of lead tetraacetate until recently had little success. Of all the not very numerous investigations we can take note only of the work [4] in which by electrochemical oxidation of lead diacetate at a platinum anode in acetic acid containing sodium acetate an 80% yield of lead tetraacetate based on the current was obtained. A necessary condition for the formation of the lead tetraacetate was the presence of 1-2% of water in the acetic acid. However, the yield of lead tetraacetate attained was maintained only for the first minutes of the electrolysis, falling after 30 minutes to 26%, and after somewhat more time, practically to zero. The reason for this phenomenon had been established previously; it consisted of the formation on the anode of a film of lead tetraacetate that shielded its surface and prevented the further oxidation of the lead diacetate. Schall and Melzer [4] worked with the electrolyte cooled to 35° and the surface of the anode cooled to 8°. At a higher temperature decomposition of the lead tetraacetate by the water present in the acetic acid occurred.

In the publication [5] the electrolysis was carried out in anhydrous acetic acid containing potassium acetate at 85°, which facilitated solution of the film of lead tetraacetate and maintenance of the high yields of it for a long time. However, in this work only the basic possiblity of accomplishing the electrooxidation of lead diacetate to the tetraacetate was established and the fundamental parameters of the process found.

In the present work a preparative method for the synthesis of lead tetraacetate has been developed on the basis of the data previously obtained.

## EXPERIMENTAL

1. Preparation of solutions. An electrolyte of the composition previously found [5] was used: 2.1 N $Pb(CH_3COO)_2$, 0.6 N $CH_3COOK$, and anhydrous acetic acid. The direction of the process and the yield of lead tetraacetate depend on careful dehydration of the acetic acid and the lead and potassium acetates. The acetic acid was dehydrated with copper sulfate, boiled with an excess of acetic anhydride for 1.5-2 hours, and distilled, whereupon a fraction was collected that distilled at 117-118°. The lead diacetate and potassium acetate were dissolved in the acetic acid thus prepared. The solution obtained was boiled with excess acetic anhydride for 5 hours, then allowed to stand for 2 days.

2. Arrangement of electrolyzer. The electrolyzer was a glass jar equipped with a coil. In the jar a ceramic diaphragm was placed across that served as a cathode area. Inside the diaphragm was another coil. It was necessary to cool because of the weak electric conductivity of the electrolyte and the considerable amounts of heat

developed when the current was passed. A nickel wire served as the cathode and a platinum mesh cylinder as the anode. The volume of the anode space was 200 ml.

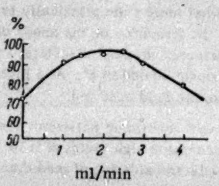
3. Separation of lead tetraacetate. The solubility of lead tetraacetate depends greatly on the temperature. On cooling to 17° more than 80% of the product precipitated from the solution. Part of the lead tetraacetate precipitated in the electrolyzer and another portion in the flask into which the electrolyte was admitted after the electrolysis. The product dried with filter paper contained 97.5% $Pb(CH_3COO)_4$. The finished product was best kept under glacial acetic acid.

The mother liquor after the electrolysis could be saturated with lead diacetate and again subjected to electrolysis. However, it must be kept in mind that the solution cannot be saturated with moist lead diacetate, since decomposition of the lead tetraacetate remaining in the mother liquor then occurs. Therefore the lead diacetate must first be dried at 50-55° for 4-6 hours and the solution should stand for 1-2 days with an excess of acetic anhydride before the electrolysis.

The amount of lead tetraacetate contained in the solution was determined iodometrically.

4. Experimental results. The electrolysis was carried out in the electrolyte for which the composition is given above. At the anode the current density was 3 amp/ $dm^2$ and the temperature was kept at 80-85° by cooling. The current strength was 2 amp. The voltage in the electrolyzer was about 100 v.

The main effort was directed toward establishment of a process procedure that guaranteed the possibility of carrying it out continously, i.e., with a circulating electrolyte. For this purpose a series of experiments was set up with different rates of circulation of the electrolyte. The relation of the yield of tetraacetate based on the current to the rate of circulation of the electrolyte is presented in the figure, from which it is apparent that the change in the yield on the basis of the current with the rate of circulation passes through a maximum at 2.5 ml/ min and reaches 95.5% under these conditions. With a load in the electrolyzer at 2 amps for 1 hour, 16 g of lead tetraacetate was produced, which amounts to 8 g per amp-hour. The expenditure of electrical energy was approximately 12 kw-hr per kg of lead tetraacetate.



Relation of yield of lead tetraacetate based on current to rate of circulation of electrolyte.

Very interesting results were obtained in attempts to replace the platinum serving as the anode material with lead peroxide prepared by a method [6] consisting of the following.

The lead peroxide reagent was built up on a foundation of perchlorovinyl fabric. Then the fabric thus treated was immersed in a saturated solution of lead nitrate. The supply of current from the positive pole of the current source was carried by means of a nickel wire woven into the fabric. A lead rod served as the cathode.

Electrolysis was carried out at room temperature and an anode current density of 0.25 (for the first four hours) – 1.0 amp/ $dm^2$. To avoid depleting the electrolyte of lead ions too rapidly as a result of their discharge at the cathode, cupric nitrate (50-80 g/ l) was added to the solution. Unfortunately, when lead peroxide was used as the anode we did not succeed in solving the problem of supplying current to it. In the place of contact of the nickel wire with the lead peroxide,evolution of heat occurred which resulted in burning of the fabric. But we succeeded in carrying out some experiments nevertheless. It was ascertained that the yield of lead tetraacetate based on the current at an anode of $PbO_2$ was the same as at a platinum anode. However, we did not succeed in solving the problem of the duration of service of a lead peroxide anode or the supplying of current to it, which appears to be a subject for further investigations.

## SUMMARY

1. A preparative method has been developed for the first time for the synthesis of lead tetraacetate by electrochemical oxidation of lead diacetate at a platinum anode.

2. The possibility has been established of carrying out this process at an anode of lead peroxide.

## LITERATURE CITED

[1] R. Krigge, Coll. "New Methods of Preparative Organic Chemistry." IL, 139 (1950).*

[2] A. Colson, C. r. 136, 575 (1903); O. Dimroth and R. Schweizer, Ber. 56, 1375 (1923).

[3] A. Colson, C. r. 136, 1664 (1903); R. Oesper and C. Deasy, J. Am. Chem. Soc. 61, 927 (1939).

[4] C. Schall and W. Melzer, Z. Electroch. 28, 474 (1922).

[5] M. Ia. Fioshin and V. A. Gus'kov, Proc. Acad. Sci. USSR, 112, 303 (1957).

[6] N. F. Razina, Diss. "Electrode Processes at a Lead Anode and Its Corrosion in the Electrolysis of Sulfuric Acid Solutions." (1955).

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*Russian translation.

# TERNARY RECIPROCAL SYSTEM OF THE BUTYRATES AND NITRATES OF SODIUM AND POTASSIUM

O. I. Dmitrevskaia

The investigation of the reciprocal system Na, K‖ $NO_3$, $C_3H_7COO$ is a part of the task of ascertaining the effect of the number of carbon atoms in the radical of a salt of a fatty acid on the process of exchange in fusions [1-3].

Sodium and potassium butyrates have been little investigated and in the reference literature it was not possible to find the heats of formation for them; it was impossible therefore to judge beforehand about the character of the system.

## EXPERIMENTAL

The investigation was carried out by the visual polythermal method of physicochemical analysis. The temperature at which the first crystals appeared was determined with the aid of a nichrome-constantine thermocouple. Chemically pure sodium and potassium nitrates were recrystallized and dried to constant weight. Sodium

TABLE 1

Binary Systems

| $C_3H_7COONa—NaNO_3$ | | $C_3H_7COOK—KNO_3$ | | $C_3H_7COONa—C_3H_7COOK$ | |
|---|---|---|---|---|---|
| mole % $NaNO_3$ | temperature | mole % $KNO_3$ | temperature | mole % $C_3H_7COOK$ | temperature |
| 0 | 330° | 0 | 404° | 0 | 330° |
| 5 | 329 | 5 | 387 | 5 | 344 |
| 10 | 325 | 10 | 370 | 10 | 355 |
| 15 | 315 | 15 | 356 | 15 | 362 |
| 25 | 283 | 20 | 342 | 20 | 370 |
| 27 | 276 | 25 | 330 | 25 | 376 |
| 30 | 274 | 30 | 320 | 30 | 380 |
| 35 | 273 | 35 | 313 | 35 | 385 |
| 40 | 271 | 40 | 306 | 40 | 388 |
| 45 | 268 | 45 | 300 | 45 | 393 |
| 50 | 267 | 50 | 294 | 50 | 396 |
| 55 | 276 | 55 | 289 | 55 | 399 |
| 60 | 283 | 58 | 283 | 60 | 401 |
| 65 | 288 | 60 | 286 | 65 | 402 |
| 70 | 292 | 65 | 291 | 70 | 403 |
| 75 | 296 | 70 | 294 | 75 | 403.5 |
| 80 | 297 | 75 | 300 | 80 | 405 |
| 85 | 298 | 80 | 306 | 85 | 405.5 |
| 90 | 300 | 85 | 314 | 90 | 401 |
| 95 | 304 | 90 | 320 | 95 | 405 |
| 100 | 308 | 95 | 328 | 100 | 404 |
| — | — | 100 | 337 | — | — |

and potassium butyrates were synthesized from chemically pure sodium and potassium bicarbonates and n-butyric acid that first had been distilled twice [4]. The melting points of the pure components were: $NaNO_3$ 308°, $KNO_3$ 337°, $C_3H_7COONa$ 330°, $C_3H_7COOK$ 404°. Polymorphic transformations in the solid state were observed for all of these salts: $KNO_3$ at 124 and 316° [5-7], $NaNO_3$ at 270° [6-8], $C_3H_7COONa$ had four transformations at 117, 232, 252, and 316° [9], and $C_3H_7COOK$ at 190, 280-285, and 345° [9].

## Binary Systems

1. The sytem $C_3H_7COOK-KNO_3$ was studied for the first time. It was characterized by a eutectic point at 283° and 58% $KNO_3$ (Table 1, Fig. 1).

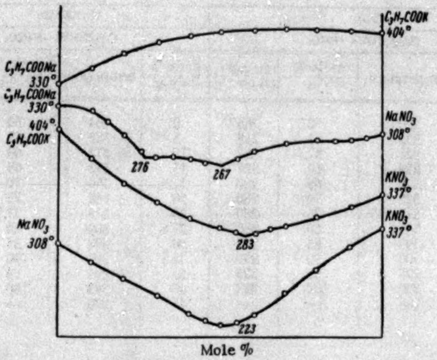

Fig. 1. Melting diagram of binary systems.

2. The system $NaNO_3-KNO_3$ has been studied by many authors [10-14]. We employed the data of reference [14]. In the system a continuous series of solid solutions is formed with a minimum m.p. at 223° and 50% $KNO_3$ (Fig. 1).

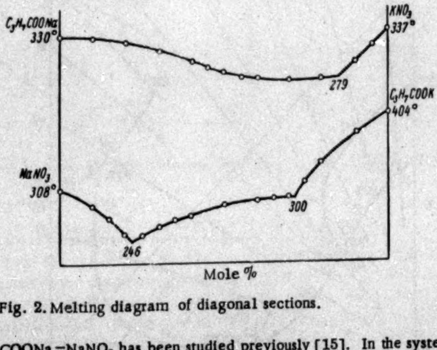

Fig. 2. Melting diagram of diagonal sections.

3. The system $C_3H_7COONa-NaNO_3$ has been studied previously [15]. In the system an incongruently melting compound is formed, probably with the composition $3C_3H_7COONa \cdot NaNO_3$. On the melting curve there are eutectic (267° and 50% $NaNO_3$) and transition (276° and 27% $NaNO_3$) points (Table 1, Fig. 1).

4. The system $C_3H_7COONa-C_3H_7COOK$ was studied for the first time. It presented a continuous series of solid solutions. The melting curve consisted of one crystallization branch without extremes (Table 1, Fig. 1).

## Diagonal Sections

1. $C_3H_7COONa-KNO_3$ is a stable diagonal with a eutectic point at 279° and 85% $KNO_3$. The $C_3H_7COONa$ branch shows a sloping region from 60 to 80% $KNO_3$, which indicates the limiting solubility of the salts of the stable pair (Table 2, Fig. 2).

### TABLE 2

Diagonal Sections

| Stable | | | | Unstable | | | |
|---|---|---|---|---|---|---|---|
| $C_3H_7COONa-KNO_3$ | | | | $C_3H_7COOK-NaNO_3$ | | | |
| mole % $KNO_3$ | temperature | mole % $KNO_3$ | temperature | mole % $NaNO_3$ | temperature | mole % $NaNO_3$ | temperature |
| 0 | 300° | 52.5 | 285° | 0 | 404° | 50 | 286° |
| 5 | 332 | 55 | 283 | 5 | 388 | 55 | 282 |
| 10 | 331 | 57.5 | 282 | 10 | 372 | 60 | 276 |
| 15 | 328 | 60 | 281 | 15 | 352 | 65 | 270 |
| 20 | 326 | 65 | 280 | 17.5 | 350 | 70 | 263 |
| 25 | 322 | 70 | 280 | 20 | 340 | 75 | 252 |
| 30 | 317 | 75 | 280 | 25 | 318 | 77.5 | 246 |
| 35 | 311 | 80 | 280 | 27.5 | 300 | 80 | 255 |
| 40 | 303 | 85 | 279 | 30 | 298 | 85 | 274 |
| 42.5 | 300 | 90 | 299 | 32.5 | 297 | 90 | 288 |
| 45 | 295 | 95 | 320 | 35 | 296 | 95 | 299 |
| 47.5 | 290 | 100 | 337 | 40 | 293 | 100 | 308 |
| 50 | 286 | — | — | 45 | 290 | — | — |

2. $C_3H_7COOK-NaNO_3$ is an unstable diagonal. The melting curve has three crystallization branches that intersect in two points: at 300° and 28.0% $NaNO_3$, and at 246° and 77.5% $NaNO_3$. The branch of the exchange products constitutes almost half of the melting curve, which indicates the distinct displacement of the equilibrium in the direction of the stable pair of salts $C_3H_7COONa$ and $KNO_3$ (Table 2, Fig. 2).

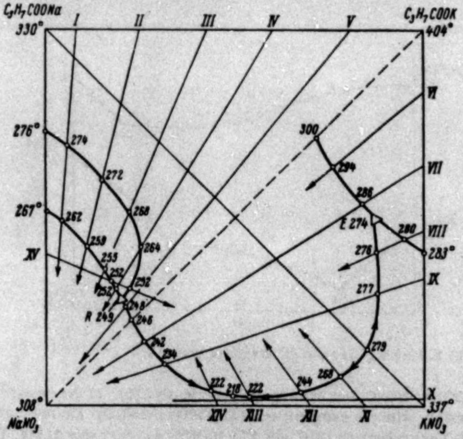
C3H7COONa
330°
I
II
III
IV
V
C3H7COOK
404°
VI
VII
VIII
IX
X
XI
XII
XIII
XIV
XV
276°
267°
308°
NaNO3
337°
KNO3
283°
274
272
268
264
262
258
255
252
252
232
R 249
248
246
242
234
222
218
222
244
268
279
277
276
E 274
280
286
294
300

Fig. 3. Position of interior sections in the reciprocal system.

## Internal Sections

15 internal sections were investigated. The direction of the internal sections is given in Fig. 3. The results of the investigation of them are presented in Figs. 4-6.

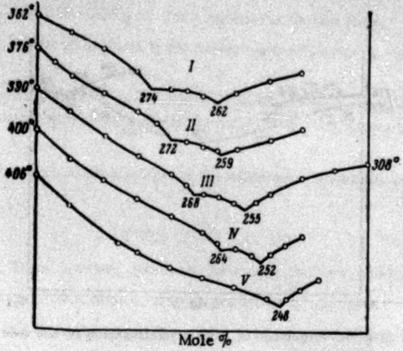

Fig. 4. Internal sections I-V of reciprocal system.

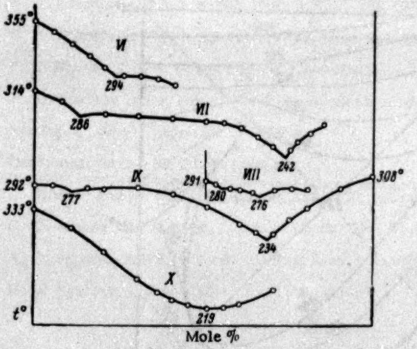

Fig. 5. Internal sections VI-X of reciprocal system.

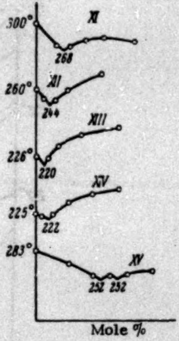

Fig. 6. Internal sections XI-XV of reciprocal system.

## Melting Diagram of Reciprocal System

From the results of the investigation of the binary systems, and the diagonal and the 15 internal sections, a projection was constructed of the curves of joint crystallization on the surface of the polytherm of the binary system $NaNO_3-KNO_3$ (Fig. 7), which permitted determining the position of the ternary and the isothermal points on the curves of joint crystallization. The projection of the diagram of the liquidus of the ternary reciprocal system on the composition square with isotherms drawn through 20° is given in Fig. 8. The system is irreversibly reciprocal with a stable diagonal. The exchange process is shifted in the direction of the stable pair $C_3H_7COONa$ and $KNO_3$. The stable diagonal is a single triangulating section dividing the square of the reciprocal system into two phase triangles: $NaNO_3-C_3H_7COONa-KNO_3$ and $KNO_3-C_3H_7COOK-C_3H_7COONa$.

The solid solutions Na, K ‖ $NO_3$ are stable in the reciprocal system up to 218°. The incongruently melting compound $3C_3H_7COONa \cdot NaNO_3$, which is formed in the binary system $C_3H_7COONa-NaNO_3$, decomposes under the influence of the butyrates and ends its existence at the point R at 249° and 19.5% $KNO_3$, 29.5% $C_3H_7COONa$, and 51% $NaNO_3$. The solid solutions Na, K ‖ $C_3H_7COO$ are stable in the reciprocal system up to 300°. In the system there is a ternary eutectic point that corresponds to: 13% $C_3H_7COONa$, 50.5% $C_3H_7COOK$, 36.5% $KNO_3$ and a temperature of 275°.

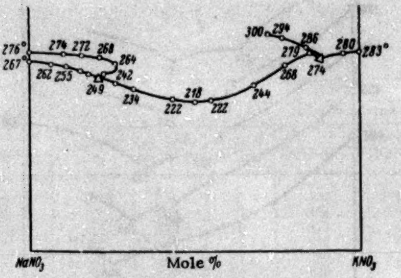

Fig. 7. Projection of joint crystallization on the side $NaNO_3-KNO_3$.

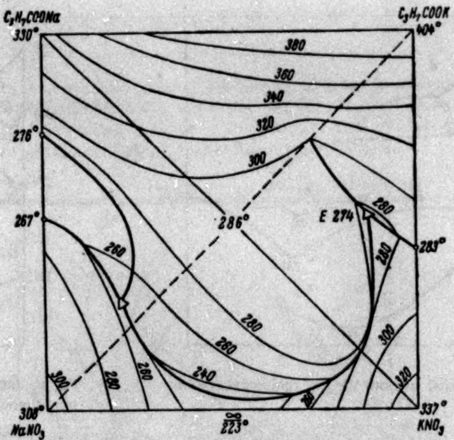

Fig. 8. Projection of the crystallization surface of the reciprocal system on the composition square.

Comparing the results for this system with the ternary reciprocal systems previously studied that had a smaller number of carbon atoms in the radical of the salt of the fatty acid [1-3], we arrive at the conclusion that with an increase in the paraffinic portion of the salts of the fatty acids there is an increase in the field of crystallization of the basic exchange product – the sodium salt of the fatty acid – and consequently an increase in the irreversibility of the reaction. Complex formation, which takes place on the lateral side of the reciprocal systems, has no effect on the direction of the exchange reaction.

## SUMMARY

1. The melting diagram of the reciprocal system, Na, K ǁ $NO_3$, $C_3H_7COO$ has been studied.

2. The system is an irreversible reciprocal one with a stable diagonal. The solid solutions, Na, K ǁ $NO_3$ are stable in the system below 218°, and the solid solutions Na, K ǁ $C_3H_7COO$ below 300°.

3. The binary system $C_3H_7COOK-KNO_3$ has been studied for the first time.

4. Complex formation, which takes place in the binary system $C_3H_7COONa-NaNO_3$, has no effect on the exchange process.

5. Comparison of the system under consideration with those previously studied shows that the irreversibility of the exchange reaction increases with an increase in the number of carbon atoms in the radical of the salt of the fatty acid.

6. In all the systems the equilibrium is shifted in the direction of formation of the sodium salt of the fatty acid.

## LITERATURE CITED

[1] O. I. Dmitrevskaia, Trans. 1st Conf. Smelensk State Med. Institute (1949).

[2] A. G. Bergman and K. A. Evdokimova, ISFKhA Acad. Sci. USSR, 26, 304 (1956).

[3] O. I. Dmitrevskaia and N. M. Sokolov, Thes. Proc. IX Conf. Smelensk State Med. Institute (1955).

[4] N. M. Sokolov, J. Gen. Chem. 26, 1582 (1956).*

[5] Tech. Encycl. Man. Phys., Chem. and Technol. Terms, 6 (1931).**

[6] A. G. Bergman and S. I. Berul', ISFKhA Acad. Sci. USSR 21, 178 (1952).

[7] V. A. Sokolov and N. E. Shmidt, ISFKhA Acad. Sci. USSR 26, 123 (1955).

[8] F. C. Kracek, J. Am. Chem. Soc. 53, 2609 (1931).

[9] N. M. Sokolov, Thes. Proc. X Conf. Smolensk State Med. Institute, (1956).

[10] Hissing, Z. phys. Chem. 32, 537 (1900).

[11] Quartoroli, Gazz. 50, 11, 64 (1920).

[12] A. Briscoe and W. Madgin, J. Chem. Soc. 123, 1608 (1923).

[13] G. Tammann, and Ruppelt, Z. anorg. Chem. 197, 67 (1931).

[14] A. G. Bergman and S. I. Berul', ISFKhA Acad. Sci. USSR 21, 179 (1952).

[15] N. M. Sokolov, J. Gen. Chem. 24, 1152 (1954).*

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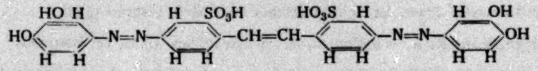
**In Russian.

# THE REACTION BETWEEN SODIUM TUNGSTATE AND STILBENE-4,4'-BIS-[(AZO-1)-3,4-DIHYDROXYBENZENE]-2,2'-DISULFONIC ACID ("STILBAZO") IN AQUEOUS SOLUTIONS

K. E. Kleiner and A. Kh. Klibus

Stilbene-4,4'-bis[(azo-1)-3,4-dihydroxybenzene]-2,2'-disulfonic acid



and its diammonium salt have been suggested, under the name "stilbazo," as reagents for the colorimetric determination of aluminum [1,2].

According to the data in the literature these reagents form colored solutions also with some other cations and complex ions. In strongly acid medium stilbazo reacts only with tungstate, molybdate, antimony, thorium, zirconium, and zirconyl ions; trivalent iron oxidizes the reagent [1]. The reaction between stilbazo and sodium tungstate is of interest as an example of a reaction between complex anions and an organic acid, and apparently it can be used for the development of a colorimetric method for the determination of tungsten. This method may prove useful, since a combination of tungsten with antimony, thorium, and zirconium is not often encountered, and tungsten can be separated from molybdenum and iron as tungstic acid.

In this article the results are reported of a photometric investigation of the reaction between sodium tungstate and stilbazo in aqueous solutions.

## EXPERIMENTAL

### Preparation of Working Solutions

Stilbazo. The commercial reagent available on the market is a poorly purified preparation of the diammonium salt. Solutions of this reagent and IREA reagent are not very stable and their reactivity diminishes even in 2-3 days after preparation. This is not associated with oxidation of the reagent, since introduction into the solutions of a reducing agent, for example hydroxylamine hydrochloride, does not stabilize them.

Reaction with tungstate, aluminum, tin, and possibly other ions goes better with the stilbazo acid than with the diammonium salt. Conversion of the salt to the acid and its simultaneous purification are based on the different solubility of stilbazo and the contaminants in methanol, methanolbenzene mixture, and strongly acid aqueous solution. Therefore we used the following method of purification. About 1 g of the ammonium salt preparation was dissolved in 250 ml of methanol. It was filtered and the filtrate was mixed with 500 ml of distilled benzene. After the brown precipitate had settled the solution was filtered through a folded filter. The filtrate was carefully evaporated to dryness on a water bath from a small porcelain dish and the dry residue was dissolved in 1.5-2 liters of distilled water. To the solution was added with stirring a sufficient amount of hydrochloric acid (1 : 1) so that a thick, blue suspension of the stilbazo acid was formed. After filtration and washing with water to remove the greater part of the hydrochloric acid, the precipitate was transferred to a watch glass and dried first at 60-70° and then in a desiccator over phosphoric anhydride. Yield 50-60%.

Aqueous solutions of this preparation were stable and were unchanged in reactivity in the course of not less than two weeks.

For colorimetric use the treatment can be limited to precipitation with hydrochloric acid from the aqueous solution of the commercial preparation.

Sodium tungstate. The initial 0.1 M solution of tungstate was prepared by solution in water of normal sodium tungstate (analytically pure). The concentration of the solution was determined by the gravimetric method as tungstic acid. The "working" solutions ($10^{-3}$ - $10^{-4}$ M) were prepared by dilution of the initial solution.

## Preliminary Experiments

Dilute aqueous solutions of stilbazo ($10^{-5}$ - $10^{-4}$ M) are yellow to orange in color, and the more concentrated ones are brown.

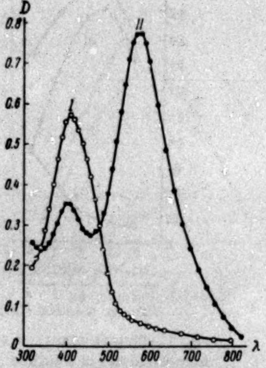


Fig. 1. Spectral characteristics of stilbazo solution (I) and of a mixture of stilbazo and sodium tungstate solutions (II) at pH 1. SF-4 spectrophotometer. 10-mm cuvette.

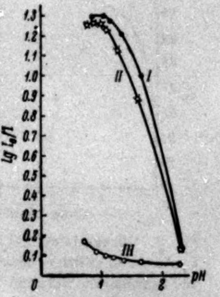


Fig. 2. Relation of optical density of mixtures of stilbazo and sodium tungstate solutions to pH. 10-mm cuvette.
I — hydrochloric acid solutions,
II — sulfuric acid solutions,
III — stilbazo solution.

In strongly acid media, stilbazo is slightly soluble; therefore upon acidification of not very dilute solutions (above $5 \cdot 10^{-5}$ M) they are colored blue or green as a result of the formation of a blue suspension of the reagent, which slowly settles out as a voluminous precipitate.

When a solution of stilbazo is mixed with a solution of sodium tungstate, the mixture is colored red-brown, blue, or blue-violet depending on the acidity and the concentration ratio of the components. The red-brown color appears at pH 2-6. The optical density of the red-brown solutions increases with a decrease in the pH from 6 to 2. The color is unstable and its intensity diminishes with time. At pH < 2 the red-brown coloration gradually changes to blue; the rate of change increases with an increase in acidity and in the concentration of the component solutions. At pH ≈ 1 the mixture of the component solutions is rapidly colored an intense blue or blue-violet. In view of the unstable color of the red-brown solutions, only the blue solutions were investigated in detail.

In Fig. 1. are shown recordings on the SF-4 spectrograph of the spectral characteristics of a solution of stilbazo ($2 \cdot 10^{-5}$ M) in hydrochloric acid (pH 1) and of a mixture containing stilbazo ($2 \cdot 10^{-5}$ M), an excess of sodium tungstate ($6 \cdot 10^{-5}$ M), and hydrochloric acid to pH 1. The tungstate was used in excess to ensure possibly more complete combination of the stilbazo in the stilbazo-tungstate compound.

The spectral characteristics of the mixture were determined 3 hours after acidification with hydrochloric acid of the mixture of the component solutions. The light absorption curves of these solutions were distinctly different, which indicates a reaction between the stilbazo and the sodium tungstate.

Furthermore, measurements of the optical density of the solutions were made on a FM universal photometer of the Pulfrich type with a M-57 light filter (effective wavelength 574 mμ).

## Relation of Optical Density to Acidity and Nature of Acid

Mixtures were made up from different volumes of $3 \cdot 10^{-4}$ M solution of stilbazo, $5 \cdot 10^{-4}$ M sodium tungstate solution,* and perchloric, hydrochloric, sulfuric, or nitric acid of a given concentration.

To accelerate the reaction it was at first carried out in a small volume (20 ml) and then after 3 hours each mixture was diluted to 60 ml with an aqueous solution of the appropriate acid with a concentration equal to its concentration in the given mixture. The final concentration of stilbazo in each mixture was $0.25 \cdot 10^{-4}$ M and that of the tungstate was $0.42 \cdot 10^{-4}$ M. The optical density was measured immediately after dilution of the solution to the greater volume; the pH was measured with a quinhydrone electrode.

In Fig. 2. the relationship of the optical density to the pH of the hydrochloric and sulfuric acid solutions is shown. The optical density increased with a decrease

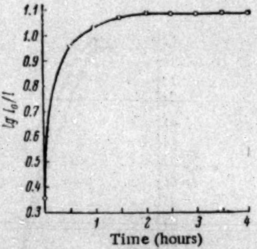


Fig. 3. Change in optical density of a mixture of stilbazo, sodium tungstate, and hydrochloric acid (pH 1) solutions with time. 10-mm cuvette.

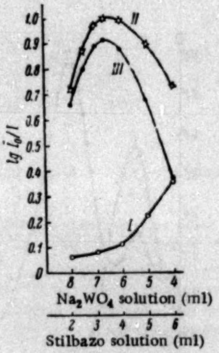


Fig. 4. Optical density of an isomolar series of solutions with a total concentration of sodium tungstate and stilbazo of $0.9 \cdot 10^{-4}$ M and pH 1. 10-10-mm cuvette. I) stilbazo solution; II) isomolar mixtures of tungstate and stilbazo solutions, III) deviation from additivity.

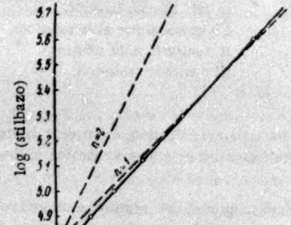


Fig. 5. Determination of the composition of the blue stilbazo–tungstate compound by the limited logarithmic method, pH 1. 10-mm cuvette. Sodium tungstate concentration $1.03 \cdot 10^{-2}$.

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* The tungstate solution was first made alkaline to phenolphthalein (see below).

in the pH to ≈ 1. At pH < 0.8 a turbidity began to form and a precipitate of stilbazo-tungstate compound separated out. For purposes of comparison the relationship of the optical density of one solution of stilbazo ($0.25 \cdot 10^{-4}$ M) to the pH in hydrochloric acid solution was used. The curves for the relation of the optical density to the pH in perchloric and nitric acid solutions almost coincide with the curve for hydrochloric acid solutions.

Thus, the optimum acidity for the formation of the blue stilbazo-tungstate compound is in the region of pH 1, therefore the further investigation was carried out with 0.1 N solutions with respect to hydrochloric acid.

### Relation of Optical Density to Time of Preparation of Component Solutions and to Order of Mixing With Acid

The optical density of solutions of the compound of stilbazo with sodium tungstate depends not only on the acidity; the length of time that the "working" tungstate solution has been prepared, its acidity before mixing with the stilbazo solution, the acid and the order of mixing the components are important.

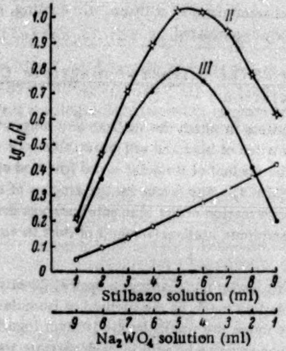

Fig. 6. Change in optical density in an isomolar series of solutions at a total concentration of sodium tungstate and stilbazo of $1 \cdot 10^{-4}$ M and pH 2. 10-mm cuvette. Light filter M53 (effective wavelength 533 mμ).
I) Stilbazo solutions; II) isomolar mixtures of tungstate and stilbazo solutions; III) deviations from additivity.

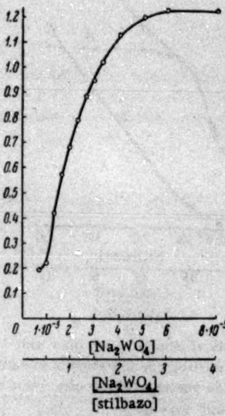

Fig. 7. Optical density of solutions with a constant starting concentration of stilbazo and varying sodium tungstate concentration, pH 1. 10-mm cuvette.

Preliminary acidification of the sodium tungstate solution resulted either in incomplete reaction if the mixing with the stilbazo solution was carried out immediately after acidification, or to the reaction's not going at all if the acidified sodium tungstate solution stood for some time before mixing. If the concentration of stilbazo was greater than $5 \cdot 10^{-5}$ M, the entire effect was the formation of a blue suspension or precipitate of stilbazo, as in the absence of tungstate. Apparently in acid medium a coarsely dispersed colloidal solution of tungstic acid is formed, which does not react with stilbazo. The reaction goes well when acid is added up to pH 1 to the previously made mixture of tungstate and stilbazo solutions. But under these conditions completeness of the reaction depends on the length of time that the tungstate solution has been prepared. The reactivity of the "working" solutions of tungstate in relation to the stilbazo diminishes approximately by half in 5 days after their preparation by dilution of the starting 0.1 M $Na_2WO_4$ solution. However, the reactivity of the tungstate solutions becomes maximum and independent of time of preparation if they are made alkaline with a solution of sodium hydroxide (to phenolphthalein). From this it follows that the form in which the tungstate solution exists apparently is of significance for the reaction between tungstate and stilbazo.

To attain the optimum conditions for the formation of the blue stilbazo–tungstate compound it is necessary first to mix the stilbazo solution with the tungstate solution that has previously been made alkaline to phenolphthalein with sodium hydroxide, and then to add hydrochloric acid to the mixture to a pH of 1.

## Relation of Optical Density to Reaction Time and Temperature

Formation of the blue stilbazo–tungstate compound occurs slowly. From Fig. 3 it can be seen that a maximum and constant value of the optical density at a concentration of $2 \cdot 10^{-5}$ M stilbazo, $4 \cdot 10^{-5}$ M tungstate, and 0.1 N hydrochloric acid is attained at room temperature in 2 hours after addition of the acid to the mixture of the component solutions. At lower concentrations of the components the rate of the reaction diminishes.

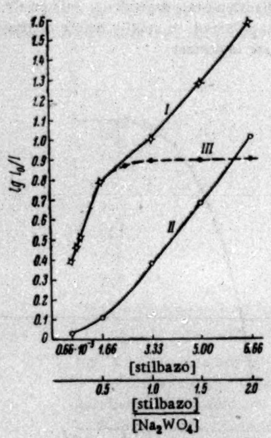

Fig. 8. Optical density of solutions with a constant starting concentration of sodium tungstate and varying stilbazo concentration, pH 1. 10-mm cuvette.
I) Mixture of tungstate and stilbazo solutions; II) stilbazo solution; III) elimination of effect of excess stilbazo.

At an elevated temperature, for example upon immersion of a test tube with the blue solution of the stilbazo – tungstate compound in boiling water, the color changes to yellow or yellow-orange, characteristic of stilbazo. On cooling, the blue color is slowly regenerated.

## Composition of the Stilbazo–tungstate Compounds in Solution

The proportions in which the stilbazo and tungstate react with the formation of blue and red-brown solutions were determined by the method of isomolar series (method of continuous changes) [3, 4]. The factor for the amount of stilbazo entering into the formation of the blue solutions was determined by a limited logarithmic method (method of shift in equilibrium) [4, 5].

In Fig. 4 are shown the changes in optical density in a series of blue solutions made by the method of isomolar series, and in Fig. 5 are shown the results by the limited logarithmic method. The concentration of acid in each mixture was 0.1 N. The optical density changed in 4 hours after addition of the acid. In Fig. 4 it is seen that the natural light absorption by stilbazo solutions (curve I) is characterized by a disproportionately large increase in the optical density upon an increase in the concentration of the reagent. This is a result, as shown above, of the formation of a blue suspension of stilbazo. In spite of this, curve II for the optical density of isomolar mixtures of stilbazo and tungstate differs distinctly from curve I. The position of the maximum in curves II and III (curve III was constructed from the data on the deviations from additivity) is at the stilbazo–sodium tungstate ratio 1 : 2. The same result was obtained when methyl alcohol, which dissolves the stilbazo suspension,* was added to the mixtures.

Experiments by the limited logarithmic method showed that one molecule of stilbazo enters into the reaction with the tungstate. This is illustrated in Fig. 5 where it is seen that the experimental points conform satisfactorily with the straight line for n = 1. Thus, the blue solutions (at pH ≈ 1) are formed when one molecule of stilbazo reacts with two molecules of sodium tungstate.

In the red-brown solutions (pH ≥ 2), in distinction from the blue ones, the maximum light absorption in the isomolar series was observed at a stilbazo : sodium tungstate ratio of 1 : 1 (Fig. 6). Thus, the red-brown color that appears at pH ≥ 2 is a result of reaction of 1 molecule of stilbazo with 1 molecule of tungstate.

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* The effect of organic solvents will be discussed in a subsequent article.

When different volumes of dark green 0.001 M stilbazo solution and a 0.01 M sodium tungstate solution acidified with hydrochloric acid to the same acidity were mixed, the pH of the mixture was practically unchanged. It can be assumed that the reaction proceeds according to the following schemes ($H_4R$ is the stilbazo molecule)

$$WO_2(OH)_2 + H_4R \rightarrow WO_2H_2R + 2H_2O, \quad (1)$$

$$WO_2(OH)_2 + WO_2H_2R \rightarrow (WO_2)_2R + 2H_2O \quad (2)$$

or with the formation of weakly dissociated tungstostilbazo acids, for example

$$H_2WO_4 + H_4R \rightarrow H_2[WO_3H_2R] + H_2O, \quad (3)$$

$$H_2WO_4 + H_2[WO_3H_2R] \rightarrow H_4[(WO_3)_2R] + H_2O. \quad (4)$$

Reaction according to schemes (2) and (4) can occur only at $pH < 2$.

Formation of the complex tungstostilbazo acids is analogous to the complex molybdenooxalic acid $H_2[MoO_3(C_2O_4)]$ [6].

## Dissociation of the Blue Compound Into the Components

In Fig. 7 are shown the changes in optical density in 0.1 N hydrochloric acid with a constant starting concentration of stilbazo ($2 \cdot 10^{-5}$ M) and varying tungstate concentration, and in Fig. 8 are shown the changes with a constant starting concentration of tungstate ($3.33 \cdot 10^{-5}$ M)and varying stilbazo concentration. Measurements of the optical density were made 4 hours after making up the mixtures. The natural light absorption with an excess of stilbazo in the mixtures was very considerable. This confirms the curve for the stilbazo solutions of corresponding concentrations. It may be considered that with a sufficient excess of stilbazo all of the tungstate is linked in the blue compound. Taking this into account, we calculated the actual excess of stilbazo in the mixtures and then, starting with the data of curves I and II, constructed curve III, in which the light absorption of the excess stilbazo is eliminated.

TABLE

Determination of the Molar Extinction Coefficient for the Stilbazo–Tungstate Compound

| Dilution to n times | Concentration of stilbazo-tungstate comp. (g-mole/l) | Thickness of cuvette (in cm) | log $I_0/I$ measured | Conversion factor | log $I_0/I$ adjusted | $\varepsilon_M$ |
|---|---|---|---|---|---|---|
| — | $16 \cdot 10^{-5}$ | 0.102 | 1.04 | | | 63730 |
| 2 | $8 \cdot 10^{-5}$ | | 0.52 | | | 63730 |
| 4 | $4 \cdot 10^{-5}$ | | 0.26 | | | 63730 |
| 8 | $2 \cdot 10^{-5}$ | | 0.13 | | | 63730 |
| 16 | $1 \cdot 10^{-5}$ | | 0.065 | | | 63730 |
| 8 | $2 \cdot 10^{-5}$ | 1.006 | 1.22 | 1.05 | 1.28 | 63620 |
| 16 | $1 \cdot 10^{-5}$ | | 0.61 | | 0.64 | 63620 |
| 32 | $5 \cdot 10^{-6}$ | | 0.31 | | 0.33 | 65610 |
| 64 | $2.5 \cdot 10^{-6}$ | | 0.15 | | 0.16 | 63620 |
| 128 | $1.25 \cdot 10^{-6}$ | | 0.075 | | 0.08 | 63620 |
| 64 | $2.5 \cdot 10^{-6}$ | 5.001 | 0.74 | 1.08 | 0.80 | 64000 |
| 128 | $1.25 \cdot 10^{-6}$ | | 0.37 | | 0.40 | 64000 |
| 256 | $6.25 \cdot 10^{-7}$ | | 0.185 | | 0.20 | 64000 |
| 512 | $3.125 \cdot 10^{-7}$ | | 0.09 | | 0.10 | 64000 |

From Fig. 7 and 8 (curve III) it follows that the blue compound is markedly decomposed in the region or equivalent (in relation to the composition of the compound) concentrations of the components. For complete suppression of the dissociation an excess of 1.5-2 times the equivalent amount of one of the components is sufficient.

## Molar Extinction Coefficient

To obtain experimental data necessary to calculate the molar extinction coefficient, a solution was prepared that contained $1.6 \cdot 10^{-4}$ M stilbazo, $4.8 \cdot 10^{-4}$ M tungstate, and hydrochloric acid (0.1 N).

3 hours after addition of the acid to this mixture it was diluted several times with a $1.6 \cdot 10^{-4}$ M solution of tungstate in 0.1 N hydrochloric acid. After each dilution the optical density was measured. A one-and-a-half times excess of tungstate ensured complete combination of the stilbazo (see Fig. 7). Thus, the concentration of the blue compound in the starting solution was $1.6 \cdot 10^{-4}$ M. The magnitude of the molar extinction coefficient was calculated by the formula

$$a_{\text{м}} = \frac{\lg I_0/I}{C \cdot l},$$

where $\log I_0/I$ is the optical density after n-times dilution, C is the concentration of the blue compound after n-times dilution, $l$ is the thickness of the cuvette layer in centimeters. The calculated and experimental data are presented in the table, from which it can be seen that the optical density of one and the same solution in different cuvettes changes disproportionately to the change in thickness of the layer. Adjusted values for the optical density were obtained by an increase in the observed values by a conversion factor. The quantity $a_M$ was calculated from the adjusted values of the optical density.

The high value for the molar extinction coefficient indicates the great sensitivity of the reaction. When optimum conditions for the reaction are maintained, it can be used for the colorimetric determination of tungsten.

## SUMMARY

1. The reaction in aqueous solution between sodium tungstate and stilbene-4,4'-bis-[(azo-1)-3,4-dihydroxybenzene]-2,2'-disulfonic acid ("stilbazo") has been investigated photometrically.

2. At pH 2 to 6 red-brown solutions are produced. The components react in the ratio, stilbazo : tungstate = 1 : 1. At pH 1 and below blue or blue-violet solutions are produced. The components react in the ratio, stilbazo : : tungstate = 1 : 2. The optimum conditions were found for the formation of the blue compound. The molar extinction coefficient is 64,000.

3. When optimum conditions are maintained for the reaction, it can be used for the colorimetric determination of tungsten.

## LITERATURE CITED

[1] V. I. Kuznetsov, G. G. Karanovich, and D. A. Drapkina, Factory Lab., 16, 787 (1950).

[2] V. I. Kuznetsov and D. A. Drapkina, Trans. All-Union Sci.-Res. Inst. Chem. Reagents, No. 21. State Chem. Press, 18 (1956).

[3] P. Job, Ann. Chim., 9, 113 (1928).

[4] A. K. Babko, Physicochemical Analysis of Complex Compounds in Solutions. Acad. Sci. USSR Press, 104, (1955).*

[5] H. Bent and C. French, J. Am. Chem. Soc., 63, 568 (1941).

[6] G. S. Savchenko, Chemistry of the Rare Elements, No. 2, 68 (1955).

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# POLAROGRAPHIC INVESTIGATION OF p-NITROSODIMETHYLANILINE

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There is little literature devoted to the polarographic reduction of nitroso compounds. Some authors have investigated: 1-nitroso-2-naphthylamine, p-nitrosodiethylaniline, p-nitrosophenol, and 1-nitroso-2-naphthol [1-4]. The polarographic reduction of N-nitrosoamines has been considered in a number of publications [5-7].

We have studied the reduction of p-nitrosodimethylaniline at a dropping mercury electrode, polarographic investigations of which we have not encountered in the literature.

## EXPERIMENTAL

The investigation was carried out with a recording SGM-8 polarograph with a galvanometer having a sensitivity of $3 \cdot 10^{-9}$ amp/mm. A capillary having the following characteristics was used for the work: $m = 1.763$ mg/sec, $\tau = 4.2$ sec in the absence of polarization voltage, $m^{2/3} \tau^{1/6} = 1.855$ mg$^{2/3}$ sec$^{-1/2}$ (when $E = -0.2$ v).

The polarographing was carried out with a background of buffered solutions of various pH values. The solutions were prepared after the pattern of the universal buffer mixtures of Britton and Robinson with the difference that while the proportion of acid to base indicated by the authors was maintained, the concentration of each of the components was increased 10 times. This permitted obtaining in the polarographing process a constant pH value and good electrical conductivity of the solution. To 9 ml of the test solution was added 1 ml of buffer mixture. Before the polarographing, air was removed with a current of hydrogen. For suppression of the maximum in the polarographic curves of p-nitrosodimethylaniline a 0.02% solution of methyl red was used. Analytically pure p-nitrosodimethylaniline was used; m.p. 77°. Aqueous solutions of the hydro-

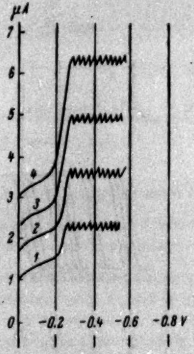


Fig. 1. Polarographic waves for p-nitrosodimethylaniline on a background of a buffer solution with pH 7.75.
Concentration of p-nitrosodimethylaniline (in millimoles/ /liter): 1) 0.06; 2) 0.12; 3) 0.18; 4) 0.24.

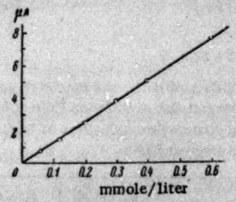


Fig. 2. Calibration line for p-nitrosodimethylaniline on a background of a buffer solution with pH 7.75.

chloride and sulfate of p-nitrosodimethylaniline served as standard solutions. The concentration of acid in these solutions was about 0.01 N.

Solutions were investigated within concentration limits from 0.06 to 0.6 millimole/liter. All determinations were carried out in an electrolyzer with an external anode — a saturated calomel electrode.

## Results of the Investigation

In Fig. 1 are presented the polarographic waves for p-nitrosodimethylaniline on a background of a buffer solution with pH 7.75 and with concentrations from 0.06 to 0.24 millimoles/liter. Similar waves were obtained for for higher concentrations — up to 0.6 millimole/liter. As can be seen from Fig. 2, the magnitude of the diffusion current is linearly related to the concentration.

TABLE 1

Magnitude of Diffusion Current at Different Concentrations of p-Nitrosodimethylaniline

| c (mmole/liter) | $I_d$ (μA) | $\frac{I_d}{c\,m^{2/3}\tau^{1/6}}$ |
|---|---|---|
| 0.06 | 0.72 | 6.47 |
| 0.12 | 1.40 | 6.30 |
| 0.18 | 2.16 | 6.47 |
| 0.24 | 2.84 | 6.38 |
| 0.30 | 3.75 | 6.74 |
| 0.40 | 4.95 | 6.74 |
| 0.60 | 7.50 | 6.74 |
| | Average . | 6.58 |

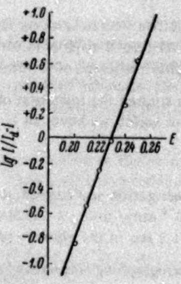


Fig. 3. Relation of $\lg \frac{I}{I_d - I}$ to E.

TABLE 2

Values of Half-wave Potentials and Magnitudes of Diffusion Current for p-Nitrosodimethylaniline at Different Background pH's.

| pH | $E_{1/2}$ (in v) | $I_d$ (μA) |
|---|---|---|
| 2.22 | +0.18 | 7.8 |
| 2.88 | +0.16 | 7.8 |
| 3.96 | +0.13 | 7.8 |
| 4.96 | +0.05 | 7.5 |
| 5.70 | —0.01 | 7.8 |
| 6.40 | —0.11 | 7.8 |
| 6.90 | —0.15 | 7.5 |
| 7.20 | —0.19 | 7.5 |
| 7.75 | —0.23 | 7.5 |
| 8.40 | —0.29 | 7.5 |
| 9.68 | —0.33 | 7.5 |
| 10.43 | —0.37 | 7.5 |

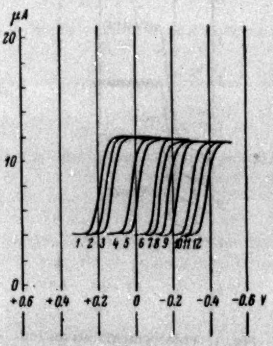


Fig. 4. Polarographic waves for p-nitrosodimethylaniline on a background of buffered solutions with various pH values for a concentration of 0.06 millimole/liter. 1) pH 2.22; 2) 2.88; 3) 3.96; 4) 4.96; 5) 5.70; 6) 6.40; 7) 6.90; 8) 7.20; 9) 7.75; 10) 8.40; 11) 9.68; 12) 10.43.

In Table 1 are presented the heights of the polarographic waves in μa, and also the diffusion current coefficients for various concentrations of p-nitrosodimethylaniline.

From the graph of the relationship of $\log \frac{I}{I_d - I}$ to E (Fig. 3) was determined the figure n. It proved to be 1.6. Apparently this indicates the irreversibility of the reduction of p-nitrosodimethylaniline at the dropping mercury cathode.

Besides the results that have been presented, we investigated the reduction of p-nitrosodimethylaniline on a background of buffer solutions with other pH values (in the range from 0.22 to 10.43). In Fig. 4 are given the polarographic waves for p-nitrosodimethylaniline on a background of solutions with various pH values for the concentration 0.60 millimole/liter. The values of the half-wave potentials and the magnitudes of the diffusion current are given in Table 2.

In the whole pH range studied only one reduction wave for p-nitrosodimethylaniline is observed. The value of $E_{1/2}$ shifts in a negative direction with an increase in the pH of the background. In acid medium the reduction proceeds in the positive region of potentials. At pH values > 6 the half-wave potential has a negative value.

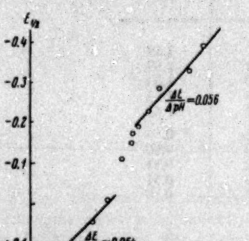


Fig. 5. Relationship of $E_{1/2}$ to pH of background.

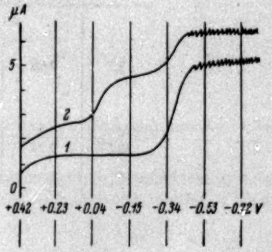


Fig. 6. Polarographic waves for p-nitrosodimethylaniline on background of 0.01 N $Na_2SO_4$. 1) 10 ml p-nitrosodimethylaniline solution, c = 0.30 millimole/liter, pH 6.3; 2) same + 0.3 ml 0.1 N $H_2SO_4$, pH 4.

However, from the graph that shows the relation of $E_{1/2}$ to pH (Fig. 5), it can be seen that, apparently, this wave is not the same in the acid and in the alkaline regions. But we were not able to obtain the two waves simultaneously in buffer solutions in the intermediate pH region (even in narrow limits).

In a nonbuffered acid solution (solution 0.01 N $Na_2SO_4$ in water with small amounts of 0.1 N $H_2SO_4$ added) two waves were obtained (Fig. 6), one of which (the first) was the result of reduction of p-nitrosodimethylaniline in acid medium, and the second was the result of reduction of p-nitrosodimethylaniline in the alkaline medium that is formed in the layer at the dropping electrode in the process of reduction of the p-nitrosodimethylaniline as a result of the participation of hydrogen ions in this process. In this instance, as seen in Fig. 6, the sum of the wave heights is equal to the height of the wave at the given concentration in neutral (or buffered) solution.

The form of the polarographic wave remains constant for all pH values with the exception of the interval between 3 and 7, where maxima are observed in the polarographic waves under the conditions investigated by us. The maxima are easily eliminated by the addition of a trifle of methyl red, after which the polarographic waves for for these pH values of the background acquire the same form as the rest of the curves.

A similar picture has been observed also for some other nitroso compounds. Thus, for example, with nitrosophenylhydroxylamine maxima are observed in the polarographic curves only at pH values < 3. At pH > 3 the maxima are not observed [5]. Apparently the presence of maxima in the indicated pH limits in the waves for p-nitrosodimethylaniline is related to the fact that its reduction potential coincides with the greatest steepness of the electrocapillary curves in the solution under consideration. The shift of $E_{1/2}$ in the direction of negative values at pH > 7 draws the p-nitrosodimethylaniline wave toward the region of the potentials of the electrocapillary maximum, in connection with which the maxima in the waves at these pH values disappear.

The height of the polarographic wave scarcely changes in the whole pH interval investigated.

We have determined the magnitude of the diffusion current for p-nitrosodimethylaniline as a function of the height of the mercury column in the reservoir both in the acid and the alkaline regions. The results of the determinations are given in Table 3.

TABLE 3

Relation of Magnitude of Diffusion Current to Pressure on the Mercury in the Capillary

| pH | C (mmole/ /liter) | $I_d$ (μA) | $h^{1/2}$ (mm) | $\frac{I_d}{h^{1/2}}$ |
|---|---|---|---|---|
| 5.7 | 0.66 | 7.8 | 4.9 | 1.59 |
| | | 8.7 | 5.49 | 1.59 |
| | | 9.6 | 5.89 | 1.63 |
| | | 10.2 | 6.29 | 1.63 |
| | | 10.8 | 6.67 | 1.63 |
| 10.17 | 0.24 | 2.40 | 4.90 | 0.49 |
| | | 2.75 | 5.49 | 0.50 |
| | | 3.00 | 5.89 | 0.51 |
| | | 3.22 | 6.29 | 0.51 |
| | | 3.34 | 6.67 | 0.50 |

From the table given it is seen that the height of the p-nitrosodimethylaniline wave both in the acid and the alkaline regions changes linearly in relation to $\sqrt{h}$. Consequently it is determined by diffusion, as this occurs in the case of the usual diffusion current.

The constance of the magnitude of the diffusion current for p-nitrosodimethylaniline for a wide range of pH values furnishes a basis for assuming the same expenditure of electrons in the reduction of this compound both in acid and in alkaline media.

From the Il'kovich equation we determined the number of electrons participating in the reduction of p-nitrosodimethylaniline. The value of the diffusion coefficient was found from the known value of the diffusion coefficient for the benzoate ion, $0.881 \cdot 10^{-5}$ cm²/sec [3, 5]. For this we employed the proportion $\frac{D_1}{D_2} = \frac{\sqrt{m_2}}{\sqrt{m_1}}$ [8]:

$$\frac{0.881 \cdot 10^{-5}}{D_2} = \frac{\sqrt{150}}{\sqrt{121}}.$$

The diffusion coefficient thus found was $D = 0.821 \cdot 10^{-5}$ cm²/sec.

Substituting the value obtained for D in the Il'kovich equation we find $n = \frac{6.58}{605 \cdot 0.821 \cdot 10^{-5}} = 3.79 \approx$ $\approx 4$, where 6.58 is the diffusion current factor $\frac{I_d}{cm^{2/3}\tau^{1/6}}$.

For the determination of n we also used a polarographic coulometric method. A detailed account of this work is given in publication [9] and also in a number of other publications [10].

The electrolyzer used by us is illustrated in Fig. 7. A sufficient amount of mercury was poured into the bottom of the electrolyzer to cover the platinum contact that was sealed in barely above the bottom of the vessel. Over the mercury was placed 1 ml of the solution under investigation containing 0.6 millimole/ liter of p-nitrosodimethylaniline (pH 9.68). Before the start of the electrolysis a current of hydrogen was passed through the solution for several minutes, after which the polarogram of the solution was taken. Then electrolysis was carried out. During this process hydrogen was passed over the solution the whole time by appropriate setting of the two-way stopcock. Repeated polarograms were taken at various intermediate times.

The number of electrons expended in the reduction of one molecule of p-nitrosodimethylaniline was calculated by the following formula [10]

$$n = \frac{4.40 \cdot 10^{-6} I_{d_0} T}{\Delta \lg I_d vc},$$

where $I_{d_0}$ is the initial magnitude of the diffusion current in μa, T is the time of electrolysis in seconds, $I_d$ is the magnitude of the diffusion current in T seconds, v is the volume of the solution in ml, and c is the concentration of the solution in millimoles/ liter.

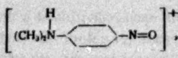
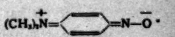
By this method we obtained the following values for n:

| T (in sec) | n |
|---|---|
| 6780 | 3.89 |
| 11880 | 4.02 |
| 14580 | 4.27 |
| Average | 4.06 |

Thus, in the reduction of a molecule of p-nitrosodimethylaniline at the dropping mercury cathode 4 electrons participate.

N. A. Izgaryshev and S. S. Kruglikov [11] reduced p-nitrosodiethylaniline electrolytically. In this case the final reaction product was p-aminodiethylaniline. The reduction of p-nitrosodimethylaniline at the dropping mercury electrode can be represented by the following equation

$$(CH_3)_2NC_6H_4NO + 4e^- + 4H^+ \rightarrow (CH_3)_2NC_6H_4NH_2 + H_2O.$$

p-Nitrosodimethylaniline enters into the reduction reaction in different form in acid and in alkaline medium. In acid medium it is in the form , and in alkaline medium it is in the form .

This is confirmed by the more intense coloration of the p-nitrosodimethylaniline solution in alkaline medium than in acid, where the electron pair on the nitrogen is bound with hydrogen, as a result of which the electron donor effect of the $N(CH_3)_2$ group is weakened.

The above-indicated condition of the p-nitrosodimethylaniline molecules in solutions with different pH values also determines their reduction potential: in alkaline medium the increased electron density at the nitroso group hinders its reduction and the reduction potential shifts to more negative values.

In buffered solutions with intermediate pH values an equilibrium between the two forms is established, apparently, very quickly, and therefore at intermediate pH values only one wave is observed for p-nitrosodimethylaniline. The half-wave potential in this case also includes the equilibrium constant between the two above-indicated forms.

p-Nitrosodimethylaniline is widely used in the manufacture of dyes. In carrying out the synthesis of p-nitrosodimethylaniline it is important to have a rapid and reliable method for determining it. Such a method is the polarographic one. It permits making the determination at any stage of the synthesis. If the synthesis of p-nitrosodimethylaniline is carried out with the observance of all the required conditions, polarographing of the filtrate after separation of the p-nitrosodimethylaniline hydrochloride gives only one polarographic wave that corresponds to the reduction of p-nitrosodimethylaniline (Fig. 8).

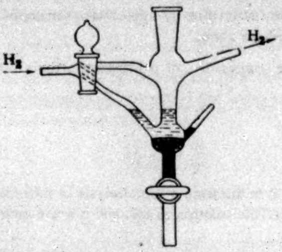


Fig. 7. Electrolyzer used for microcoulometric determination of n.

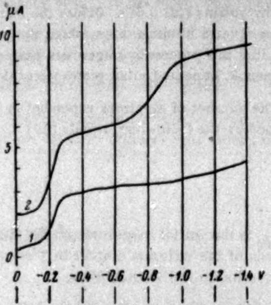


Fig. 8. Polarograms of the reaction mixture during the synthesis of p-nitrosodimethylaniline. 1) with correct synthetic procedure; 2) with disruption of correct synthetic procedure.

If the correct procedure for the synthesis is disrupted, for example if the sodium nitrite solution is not added slowly enough to the aniline hydrochloride solution, when the filtrate is polarographed, besides the wave for p-nitrosodimethylaniline there is also found a second wave with a more negative reduction potential that corresponds to the reduction of one of the side products of the reaction not foreseen in the synthetic process.

The use of the colorimetric method in this case is unreliable, since a yellow color of the solution is produced not only by the basic reaction product p-nitrosodimethylaniline, but also by by-products of the reaction.

## SUMMARY

1. The polarographic behavior of p-nitrosodimethylaniline has been studied. Its basic polarographic constants have been determined.

2. It has been found that p-nitrosodimethylaniline upon reduction at a dropping mercury electrode forms two polarographic waves, each of which appears at a certain pH value: the first in acid solutions and the second in in alkaline solutions. On a background of unbuffered acid solutions the two waves are obtained simultaneously.

3. The mechanism of reduction of p-nitrosodimethylaniline has been investigated and the number of electrons participating in the reduction reaction has been determined by two methods. The number is four.

4. It has been shown that it is practical to use the results obtained for the quantitative determination of p--nitrosodimethylaniline in the process of its synthesis.

## LITERATURE CITED

[1] A. Okac and L. Gracova, Chem. Listy. 47, 367 (1953).

[2] S. Kikuchi, J. Sakaguchi and K. Honda, Chem. Listy 25, 98 (1952).

[3] M. J. Astle and W. V. McConnel, J. Am. Chem. Soc. 65, 35 (1943).

[4] R. Wilson, and H. Lovelady, Anal. Chem. 27, 1231 (1955).

[5] I.M. Kolthoff and A. Liberti, J. Am. Chem. Soc. 70, 1885 (1948).

[6] C. Calzolari and A. Donda, Ann. Chim. (Rome) 44, 356 (1954).

[7] R. Bruce Martin, and M. O. Tashdjian, J. Phys. Chem. 60, 1028 (1956).

[8] Ia. P. Gokhshtein, Trans. Committee on Analyt. Chem., Vol. II (V). Acad. Sci. USSR Press, 5 (1949).

[9] A. G. Stromberg and T. M. Markacheva, J. Phys. Chem. 28, 671 (1954).

[10] L. Meites, Polarographic Techniques N. Y., 223 (1955).

[11] N. A. Izgaryshev and S. S. Kruglikova, Proc. Acad. Sci. USSR, 94, 913 (1954).

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# THE POLAROGRAPHIC DETERMINATION OF SOME DERIVATIVES OF 2-ETHYLANTHRAQUINONE

L. M. Shtifman, S. V. Siavtsillo, and L. G. Kuriakova

A number of studies have been devoted to the problem of the polarography of compounds of the anthraquinone series.

The reduction potential of anthraquinone in a water-alcohol solution in the presence of 0.2 N tetramethylammonium hydroxide was first determined by H. Adkins and F. Cox [1]; these authors obtained a value for the half-wave potential of anthraquinone equal to −0.6 v with respect to a saturated calomel electrode. Iu. I. Vainshtein [2] worked out a polarographic method for the quantitative determination of benzanthrone in the presence of anthraquinone in 80% methyl alcohol which contained 0.1 N $H_2SO_4$. According to his data, the half-wave potential for anthraquinone was −0.36 v. A polarographic study of the hydroxy derivatives of anthraquinone (alizarine, quinalizarine, anthrarufine and others) in an alkaline medium at pH 10-12 in the presence of ammonia, phosphate, and borate buffers was carried out by N. Furman and K. Stone [3]. These authors observed that for these compounds they obtained a normal wave, suitable for quantitative determination of the substances. A. M. Vasil'ev and A. I. Kostromin [4] determined the half-wave potential of quinalizarine (1,2,5,8-tetrahydroxyanthraquinone) in an ammonia medium (0.25 N) on a base of ammonium nitrate; they observed two waves, and the height of the first wave, whose half-wave potential was −0.78 v (with respect to a saturated calomel electrode), changed linearly with change in quinalizarine concentration. Therefore the authors recommended carrying out a quantitative determination of this substance by the first wave. K. Stone and N. Furman [5] studied the polarography of anthrone and 10-methyl-10-hydroxyanthrone dissolved in dioxane in the presence of acetate, phosphate, and borate buffers. They established that at pH 7.0-8.2 the half-wave potential of anthrone varied from −0.85 to −0.89 v, and for 10-methyl-10-hydroxyanthrone the half-wave potential varied from −1.1 to −1.27 v. They showed that in a medium of 0.1 N KCl at pH 7.1 the half-wave potential of 10-methyl-10-hydroxyanthrone was −1.29 v. R. Day and J. Kirkland [6] studied anthrone polarographically and observed that in aqueous alcohol solution at different pH values one or two anthrone waves were found. At pH 6.9 they found one wave with a half-wave potential of 1.26 v.

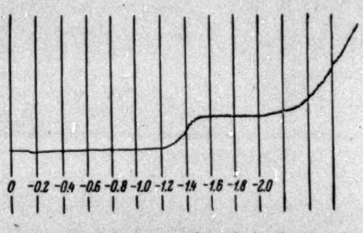

Fig. 1. Polarogram of 2-ethylanthrone.

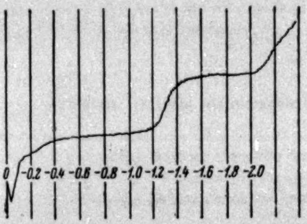

Fig. 2. Polarogram of 2-ethyl-10-hydroxyanthrone.

In the present work we have studied polarographically the 2-ethylanthraquinone derivatives: 2-ethylanthrone and 2-ethyl-10-hydroxyanthrone. 2-Ethylanthrone was synthesized by the method described earlier [7]. The substance forms white needles with m.p. 60-62°.

Found %: C 86.39; H 6.40. $C_{16}H_{14}O$. Calculated %: C 86.50; H 6.30.

2-Ethyl-10-hydroxyanthrone was obtained by bromination of ethylanthrone and oxidation of 2-ethyl-10-bromoanthrone [7]; m.p. 92-93°.

Found %: C 80.5; H 6.1. $C_{16}H_{14}O_2$. Calculated %: C 80.7; H 5.9.

We submitted 0.001-0.01 M solutions of 2-ethylanthrone and 2-ethyl-10-hydroxyanthrone to polarography. Because of their poor solubility in aqueous alcohol, the compounds were dissolved in benzene and to 1 ml of the benzene solution was added 5 ml of a 3 M water solution of tetramethylammonium bromide and the resulting mixture was diluted to 25 ml with 80% aqueous methyl alcohol. Thus, the polarogram was taken on a base of 0.6 M$[(C_2H_5)_4N]$Br in a mixture which contained about 61 volume % of methyl alcohol, 35 volume % of water, and 4 volume % of benzene; the pH of the solution lay between 7.0 and 7.5.

The polarography was carried out in the "Geological Survey" polarographic plant (Leningrad). The measurements were made at a temperature of 25 ± 0.5°. The capillary constant was $m^{2/3}\, t^{1/6} = 0.94$ mg$^{2/3}$ sec$^{1/6}$ where $m$ is the weight of mercury passing from the capillary per second and $t$ is the period of dropping. The sensitivity of the galvanometer was $10^{-9}$ a/mm. The electrode for comparison was a saturated calomel half-element. The half-wave potential was determined by the graphical method of Gon. The resulting polarograms are given in Figs. 1 and 2.

TABLE

Relation of Height of Wave (h) to Concentration (c)

| c (in mg/ml | h (in mm) |
|---|---|
| **2-Ethylanthrone** | |
| 1.010 | 6 |
| 2.024 | 13 |
| 3.036 | 18 |
| 4.048 | 23 |
| **2-Ethyl-10-hydroxyanthrone** | |
| 4.3 | 15.8 |
| 8.6 | 31.8 |
| 12.9 | 47.5 |
| 17.2 | 62.0 |

The half-wave potential for 2-ethylanthrone determined under these conditions was −1.4 ± 0.03 v. For 2-ethyl-10-hydroxyanthrone the half-wave potential measured under the same conditions was −1.3 ± 0.03 v.

Special experiments were carried out to show that when benzene solutions of 2-ethylanthrone stood for several weeks, the height of its wave did not change. Under the same conditions, for solutions of 2-ethyl-10-hydroxyanthrone we found a decrease in the height of the wave from the half-wave potential of −1.3 v and the appearance of a wave with half-wave potential −0.7 v which corresponded to 2-ethylanthraquinone; this could be explained by tautomeric change of 2-ethyl-10-hydroxyanthrone into 2-ethylanthrahydroquinone with its subsequent oxidation to 2-ethylanthraquinone.

For 2-ethyl-10-hydroxyanthrone and for 2-ethylanthrone we established a straight line relationship between height of wave (h) and concentration of substance (c) in the solution. The data are given in the Table.

The same relationship is preserved in the presence of 2-ethylanthraquinone (m.p. 199°) and 1,2,3,4-tetrahydro-2-ethylanthraquinone (m. p. 169°).

It follows from the Table that the content of 2-ethyl-10-hydroxyanthrone and 2-ethylanthrone in solution can be determined polarographically.

## SUMMARY

1. We have determined the half-wave potentials of 2-ethylanthrone and 2-ethyl-10-hydroxyanthrone in a base of 0.6 M of tetramethylammonium bromide in aqueous methyl alcohol solution which contains a small amount of benzene. The half-wave potentials of these compounds are 1.4 and 1.3 v respectively (with respect to a saturated calomel electrode).

2. We established a linear relation between height of wave for 2-ethylanthrone and 2-ethyl-10-hydroxyanthrone and their concentrations within the limits of 0.001-0.01 M solutions.

## LITERATURE CITED

[1] H. Adkins and F. Cox, J. Am. Chem. Soc. 60, 1151 (1938).

[2] Iu. I. Vainshtein, Zav. Lab. 15, 411 (1949).

[3] N. Furman and K. Stone, J. Am. Chem. Soc., 70, 3055 (1948).

[4] A. M. Vasil'ev and A. I. Kostromin, Uch. Zap. Kazansk. G.U., No. 4, 112 (1952-1953).

[5] K. Stone and N. Furman, J. Am. Chem. Soc. 70, 3062 (1948).

[6] R. Day and J. Kirkland, J. Am. Chem. Soc. 72, 2766 (1950).

[7] S. V. Slavtsillo, V. I. Savushkina and E. M. Zhernovskaia, Zh. O. Kh. 28, 1758 (1958).*

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# CYCLOALKYLATED AROMATIC COMPOUNDS XV. THE CONDENSATION OF FLUORENE WITH CYCLOHEXANOL IN THE PRESENCE OF ALUMINUM CHLORIDE

N. G. Sidorova and G. Kh. Tyshchuk

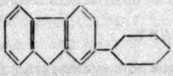
In one of our preceding works [1] we described the condensation of fluorene with cyclohexanol in the presence of $AlCl_3$. The reaction product was a cyclohexylfluorene of unknown structure with m.p. 133°. In the present work we have continued the study of this reaction and investigated the condensation product.

In seeking the best conditions of alkylation, we have carried out several condensations with different amounts of $AlCl_3$ and equimolecular ratios of fluorene to cyclohexanol. However, we did not succeed in increasing the yield obtained in the previous work: both increase and decrease in the amount of $AlCl_3$ produced a lower yield of alkylation product. The maximum yield of crude cyclohexylfluorene (32.9%) was obtained with 0.85 g equiv. of $AlCl_3$. Along with the alkylation reaction there occurred a dehydration of the cyclohexanol and a polymerization of the cyclohexene which was formed. This explains the need for using a large amount of cyclohexanol.

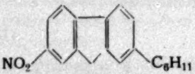
For the determination of the position of the substituting group in the cyclohexylfluorene we oxidized it with dilute $HNO_3$ at 140-150° in a sealed tube of 2-fluorenonecarboxylic acid whose methyl ester is described in the literature.

Dehydrogenation of cyclohexylfluorene over platinized charcoal gave a new product, 2-phenylfluorene.

Both these reactions positively determined the structure of the condensation product as 2-cyclohexylfluorene (I).



(I)



(II)

To characterize the new hydrocarbon we prepared the mononitro compound from it. Since all reactions of electrophilic substitution in the fluorene molecule go into positions 2 and 7, then this substance evidently must have the structure of 2-nitro-7-cyclohexylfluorene (II).

Both cyclohexylfluorene and phenylfluorene form picrates, but they are so unstable that we could not isolate them in pure form.

## EXPERIMENTAL

Condensation of fluorene with cyclohexanol was carried out by the method described earlier [1]. The cyclohexylfluorene was collected as the fraction with b.p. 175-200° at 3 mm. In the residue, a thick, glassy mass of a dark yellow color, were polymers of cyclohexene. The conditions and results of the condensation are given in the table.

For purification the cyclohexylfluorene was twice vacuum-distilled and then recrystallized several times from alcohol. Cyclohexylfluorene forms very fine crystals with m.p. 133°. It sublimes in the form of needles.

| Mole ratio $C_{13}H_{10}$ : $C_6H_{11}OH$ : $AlCl_3$ | Time of heating (in hours) at temperature |  | Yield of crude cyclohexylfluorene (in %) |
|---|---|---|---|
|  | 65-80° | 95-100° |  |
| 1 : 1 : 0.73 | 7 | 10 | 22.3 |
| 1 : 1 : 0.85 | 8 | 12 | 32.9 |
| 1 : 1 : 1 | 7 | 16 | 21.9 |

Oxidation of cyclohexylfluorene. 1 g of the hydrocarbon and 100 ml of nitric acid (d 1.1) were heated in a sealed tube in a Carius furnace at 140-150° for 7 hours. The resulting yellow precipitate was filtered off, dissolved in soda, the solution was filtered, and 2-fluorenonecarboxylic acid was precipitated from the filtrate by concentrated hydrochloric acid. After recrystallization from alcohol it melted at 330-333° with sublimation and decomposition.

Methyl 2-fluorenonecarboxylate was obtained by heating on the water bath 0.25 g of the acid and 30 ml of methyl alcohol with several drops of concentrated $H_2SO_4$ for 2 hours. It was purified by vacuum distillation. Yellow needles with m.p. 181°.

According to the literature, 2-fluorenonecarboxylic acid melts at 330° with sublimation and decomposition [2], and its methyl ester melts at 181° [3].

Dehydrogenation of cyclohexylfluorene. 0.5 g of cyclohexylfluorene and 0.05 g of 20% platinized charcoal were heated in a hard glass test tube on a sand bath at 300-330° until evolution of hydrogen stopped.

The reaction product was removed with benzene and after the solvent had been distilled off, was purified by sublimation in a vacuum with subsequent recrystallization from alcohol. Phenylfluorene was obtained in the form of colorless, glittering plates with m.p. 193-194°.

Found %: C 94.10; H 5.80. $C_{19}H_{14}$. Calculated %: C 94.18; H 5.82.

Nitration of cyclohexylfluorene. To 0.1 g of hydrocarbon dissolved in 40 ml of warm glacial acetic acid was added 1 ml of $HNO_3$ (d 1.42) with stirring for 15 minutes. Then the reaction mixture was heated at 80° for 5 minutes and after cooling was poured onto ice. The resulting precipitate was filtered off, washed with water, dried and recrystallized from alcohol. 2-Nitro-7-cyclohexylfluorene was isolated in the form of yellow needles with m.p. 150-150.5°.

Found %: N 4.76. $C_{19}H_{19}O_2N$. Calculated %: N 4.78.

## SUMMARY

1. We have showed that in the condensation of fluorene with cyclohexanol in the presence of $AlCl_3$, 2-cyclohexylfluorene is formed.

2. When 2-cyclohexylfluorene is dehydrogenated it gives 2-phenylfluorene, and when it is nitrated, it gives 2-nitro-7-cyclohexylfluorene.

## LITERATURE CITED

[1] N. Sidorova and I. A. Poliker, Zh. O. Kh. 28, 1276 (1958).*

[2] D. C. Morrison, Ch. A. 48, 3314 (1954).

[3] Beilst., X, 774.

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# RADICAL AND IONIC ALKYLATION OF THE AROMATIC RING

## VII. BUTYLATION OF BENZENE, NAPHTHALENE, PHENOL, AND ANISOLE

S. G. Mel'kanovitskaia and I. P. Tsukervanik

In the previous communication [1] it was shown possible to use a copper catalyst for the alkylation of aromatic compounds by benzyl chloride and diphenylchloromethane. On the basis of these results we have assumed that this reaction proceeds homolytically, but without the formation of free radicals. The present work is devoted to explaining the characteristics of the alkylation of different compounds by n-butyl chloride in the presence of copper. For comparison we studied the free-radical butylation of anisole. As a source of free butyl radicals we used n-butylphenyltriazene.

In distinction to the benzylation reactions with diphenylchloromethane, butylation in the presence of copper goes with more difficulty and requires a higher temperature (200-250°). When n-butyl chloride acts on benzene, naphthalene, phenol, and anisole, it gives the corresponding mono- and dibutyl aromatic compounds, and in reaction with phenol it also gives the butyl ether of butylphenol. No other products were observed in these reactions. In all cases sec-butyl derivatives were formed.

Isomerization of the alkyl groups in butyl and dibutylbenzene was shown by the method of perbromination [2]. The para position of the butyl radicals in dibutylbenzene was determined by oxidation with chromic mixture to terephthalic acid.

The introduction of the butyl group in the para position in phenol was shown by oxidation of the methyl ether of the resulting butylphenol with 7% $HNO_3$ according to Nazarov [3]. To show that the isolated product was p-sec-butylphenol, we ran another synthesis: sec-butylbenzene was sulfonated and the sulfonate salt was fused with KOH [4]. From the butylphenol preparations we obtained in the usual way [5] butylphenoxyacetic acid which was transformed into the toluidide with m.p. 90-91°. The identity of both p-toluidides of p-sec-butylphenoxyacetic acid was shown by absence of depression of a mixed melting point.

It is often thought [6] that in the alkylation of phenols in the presence of acid catalysts ($AlCl_3$,$BF_3$) the first step is the formation of an ether which can then be alkylated, split, and isomerized into the substituted phenol. Since we also obtained the butyl ether of butylphenol, it was interesting to explain the course of this reaction.

We showed that isomerization of the specially synthesized sec-butylphenyl ether under the conditions of the experiments proceeded only under the influence of HCl. We isolated a butylphenol fraction (25%). When we obtained the derivative with chloroacetic acid [5], we isolated crystalline butylphenoxyacetic acid with m.p. 112-113° whose toluidide melted at 70-71°.

It is known that isomerization of alkylphenols under the influence of acid catalysts usually gives a mixture of o- and p-alkylphenols. Since p-sec-butylphenol gave an oily sec-butylphenoxyacetic acid whose toluidide melted at 90-91°, we assume that the butylphenoxyacetic acid with m.p. 112-113° is a derivative of o-sec-butylphenol.

These results allow us to consider the main direction of the reaction of n-butyl chloride with phenols in the presence of copper as a direct alkylation of the ring, since the product isolated in this case is p-sec-butylphenol.

$$C_4H_9Cl + C_6H_5OH \rightarrow C_4H_9C_6H_4OH + HCl$$

The formation of p-sec-butylanisole in the reaction of butylation of anisole was shown by splitting it with hydriodic acid to p-sec-butylphenol, which was characterized by the above method. In the thermal butylation of benzene, naphthalene and phenol by n-butyl chloride we also isolated butyl derivatives. We showed the formation of p-sec-butylbenzene and o-sec-butylphenol.

Free radical butylation of anisole with small yield (8.5%) was established by the thermal decomposition of n-butylphenyltriazene in it. To show its structure, the butylanisole was split to the corresponding butylphenol. With chloroacetic acid the butylphenol gave a mixture of crystalline butylphenoxyacetic acids from which fractional crystallization separated only one isomer, with m.p. 105-106°, in pure form. The conclusion that this acid corresponded to o-n-butylphenol followed from the results of a comparison of our butylphenoxyacetic acid with the literature data for the derivatives from different isomers of butylphenol (see Table 4). The presence of p-butylanisole was shown by oxidation with 7% $HNO_3$ [3] to form anisic acid.

Along with butylanisole we obtained: aniline (38.5%), N-n-butylaniline (22.2%), p-n-butylaniline (11.1%). In the gaseous products we observed saturated and olefinic hydrocarbons. The scheme of free radical butylation which we give is analogous to the scheme of free radical substitution of hydrogen in the aromatic ring given by Kooyman [7], Schwartz [8], and Waters [9].

$$\begin{gathered}
C_4H_9NHN{=}NC_6H_5 \rightleftarrows C_4H_9N{=}NNHC_6H_5 \\
C_4H_9N{=}NHNC_6H_5 \rightarrow C_4H_9\cdot + N_2 + C_6H_5NH\cdot \\
C_4H_9\cdot + C_6H_5OCH_3 \rightarrow (C_4H_9C_6H_5OCH_3)\cdot \\
(C_4H_9C_6H_5OCH_3)\cdot + C_6H_5NH\cdot \rightarrow C_4H_9C_6H_4OCH_3 + C_6H_5NH_2 \\
C_4H_9\cdot + C_6H_5NH_2 \rightarrow (C_4H_9C_6H_5NH_2)\cdot \\
(C_4H_9C_6H_5NH_2)\cdot + C_6H_3NH\cdot \rightarrow C_4H_9C_6H_4NH_2 + C_6H_5NH_2 \\
C_4H_9\cdot + C_6H_5NH\cdot \rightarrow C_6H_5NHC_4H_9 \\
C_4H_9\cdot \rightarrow C_4H_8 + C_4H_{10}
\end{gathered}$$

Comparison of the results of free radical butylation with those of butylation in the presence of copper (yield of butyl derivatives, absence or presence of isomerization of the butyl group, variety of side products) leads us to the conclusion that the mechanism of butylation in the presence of copper is analogous to that which we have assumed for benzylation and the reaction with diphenylchloromethane (1). There is homolysis in the reaction complex without formation of free radicals.

## EXPERIMENTAL

### Butylation of Benzene, Naphthalene, Phenol, and Anisole in the Presence of Copper

The reaction of butylation of benzene, naphthalene, phenol and anisole in the presence of copper was carried out in an acid resistanct autoclave (with a needle valve) or in sealed ampules placed in an autoclave with a solvent.

The product of butylation of benzene was separated by fractionation after filtration of the solid residue.

For isolation of the butylnaphthalene compound from the mixture with naphthalene we attempted to sublime the naphthalene or steam distil it, but these methods did not give a good separation; therefore the mixture was distilled into wide fractions: naphthalene 210-250° and butynaphthalene 25-280°. The content of butylnaphthalene in the naphthalene reaction was determined by the temperature of solidification [10]. We first constructed a curve showing the relation of melting point of the mixture of naphthalene and butyl naphthalene fractions to the content of the components.

The butylation products of phenol and anisole were treated with 15% NaOH solution to separate the phenols and ethers.

For separation of the individual substances in all cases we carried out repeated distillations of similar fractions from analogous experiments on a column with an effectiveness of 6-8 theoretical plates.

The conditions of the separate experiments, amounts of starting substances, and yields of butylaromatic compounds are given in Table 1. The physical constants of the resulting substances and the melting points of their derivatives are given in Table 2.

TABLE 1

Butylation of Benzene, Naphthalene, Phenol, and Anisole

| Starting substance (g) | | | | Molecular ratio $C_4H_9Cl$ : ArH : Cu | Reaction conditions | | Butylaromatic compound (in g) | | Tar (in g) |
|---|---|---|---|---|---|---|---|---|---|
| n-Butyl chloride | Aromatic compound | | Copper | | Temp. | Duration (hours) | Mono- | Di- | |
| 8.8 | Benzene | 8.9 | – | 1 : 1.2 | 300° | 10 | 2.2 | 0.4 | 0.4 |
| 6.6 | The same | 7.2 | 0.45 | 1 : 1.2 : 0.1 | 205 | 15 | 2.7 | 1.2 | 0.2 |
| 3.3 | Naphthalene | 9.3 | – | 1 : 2 | 250 | 7 | 0.54 | – | 0.2 |
| 10 | The same | 13.9 | 0.7 | 1 : 1 : 0.1 | 250 | 7-8 | 7.96 | 6.36 | 0.7 |
| 10 | The same | 27.8 | 0.7 | 1 : 2 : 0.1 | 250 | 7-8 | 15.14 | 1.1 | 1.5 |
| 5.1 | Phenol | 10.2 | – | 1 : 2 | 250 | 6 | 0.95 | 0.4* | 0.3 |
| 5.1 | The same | 10.2 | 0.35 | 1 : 2 : 0.1 | 200 | 6 | 4.1 | 0.7* | 0.3 |
| 4.1 | The same | 8.2 | 0.28 | 1 : 2 : 0.1 | 250 | 6 | 4 | 0.55* | 0.8 |
| 5 | Anisole | 11.7 | 0.35 | 1 : 2 : 0.1 | 180-200 | 6 | 2.5 | 0.9** | 0.3 |

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*Butyl ether of butylphenol.

**Butylphenol was formed because of partial splitting of butylanisole by HCl which was formed.

TABLE 2

Physical Constants of Butyl- and Dibutylaromatic Compounds and Melting Points of Their Derivatives

| Name of compound | Boiling point | Pressure (in mm) | $d^{20}_4$ | $n^{20}D$ | Name of derivative | Melting point of derivative | Literature |
|---|---|---|---|---|---|---|---|
| sec-Butylbenzene | 168-169° | 719 | 0.8620 | 1.4890 | 2,4-Diacetamino-sec-butylbenzene | 189-190° | [14],<br>[15], |
| | | | | | Hexabromobenzene | 319-321 | [2], |
| Di-p-sec-butylbenzene | 227-333 | 719 | 0.8594 | 1.4885 | Dimethyl ester of terephthalic acid | 140-141 | [16] |
| | | | | | Hexabromobenzene | 320-323 | [2] |
| α-sec-Butylnaphthalene | 141 | 13 | 0.9800 | 1.5835 | Picrate | 76-78 | [17] |
| Dibutylnaphthalene | 177-183 | 14 | 0.9539 | 1.5630 | – | | |
| p-sec-Butylphenol* | 123-124 | 14 | 0.9777 | 1.5209 | p-Toluidide of p-sec-butylphenoxyacetic acid | 89-91 | [18] |
| Butyl ether of butylphenol | 145-147 | 12 | 0.9436 | 1.5119 | – | – | |

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*Crystallized with difficulty, m.p. 55-59°.

Obtaining the methyl ether of p-sec-butylphenol. 2.1 g of dimethyl sulfate was added to 5 g of sec-butylphenol in 8 ml of 20% NaOH solution with energetic shaking, and the mixture was heated 7-8 hours on the water bath. We obtained 3.6 g with b.p. 103° at 15 mm, $d^{20}_4$ 0.9389, $n^{20}D$ 1.5035 [11].

Oxidation of the methyl ether of p-sec-butylphenol. 0.2 g of the substance and 5.5 ml of 7% $HNO_3$ were heated in a sealed ampule (placed in an autoclave with benzene) for 2 hours at 180-200°. The product was twice extracted with ether, the ether extract was washed with water and was extracted with a solution of $K_2CO_3$. The extract was acidified with hydrochloric acid and twice extracted with ether. We obtained 0.07 g of anisic acid with m.p. 179-182° [12].

Obtaining p-sec-butylphenoxyacetic acid. 3 g of p-sec-butylphenol was dissolved in 12 ml of 33% NaOH, 8 ml of a 50% solution of chloroacetic acid was added, and the mixture was heated on the water bath for 1.5-2 hours. After the usual treatment [5] 2.9 g of oil separated which could not be crystallized.

TABLE 3

Products Isolated in the Deomposition of n-Butylphenyltriazene in Anisole

| Name of compound | Yield (in g) | Boiling point | Pressure (in mm) | $n^{20}_D$ | Name of derivative | Melting point of derivative | Literature |
|---|---|---|---|---|---|---|---|
| o- and p-Butylanisoles | 0.95 | 105-120° | 22 | 1.5100 | o-n-Butylphenoxyacetic acid | 105-106° | |
| | | | | | p-Methoxybenzoic acid* | 173-178 | [12] |
| Aniline | 1.85 | 180-185 | 725 | 1.5714 | Hydrochloride | 195 | [23] |
| N-n-Butylaniline | 1.7 | 125-127 | 22 | 1.5360 | The same | 112-114 | [24] |
| p-n-Butylaniline | 0.85 | 220-235 | 720 | 1.5450 | p-Acetamino-n-butylbenzene | 103-104 | [15] |

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* The product was oxidized by 7% $HNO_3$ at 180-200°

TABLE 4

Melting Points of Butylphenoxyacetic Acids and Their Toluidides

| Isomers of butylphenol | Melting points | |
|---|---|---|
| | Butylphenoxyacetic acid | Toluidide of buylphenoxyacetic acid |
| o-n-Butylphenol . . . . . . . . . . . . . . . . | 105-106 | – |
| o-sec-Butylphenol . . . . . . . . . . . . . . . | 112-113 | 70-71* |
| p-n-Butylphenol . . . . . . . . . . . . . . . . | 81* | (100-103)** |
| p-sec-Butylphenol . . . . . . . . . . . . . . . | (61-63)** | 90-91 |

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* Literature data [25].

** The melting points in parentheses are for substances which were not fully purified and were not analyzed. We usually worked with oily p-sec-butylphenoxyacetic acid. Crystallization took place after long standing.

Obtaining p-sec-butylphenoxyacetic acid p-toluidide. 1.8 g of the acid in alcohol solution was neutralized with 1 N NaOH to phenolphthalein, the solution was evaporated and the resulting 2 g of the sodium salt was fused with 5 g of p-toluidine (1.5 ml of concentrated hydrochloric acid was added to the mixture) in a hard glass test tube at 120-130° for 1.5 hours. The product was treated with dilute hydrochloric acid. We obtained 0.95 g of a crystalline substance which after purification from aqueous alcohol was obtained in the form of glittering plates with m.p. 89-91°.

Found %: C 76.54; H 7.82; N 4.74. $C_{19}H_{23}O_2N$. Calculated %: C 76.76; H 7.8; N 4.71.

Isomerization of sec-butylphenyl ether under the influence of HCl. sec-Butylphenyl ether was synthesized according to Smith [13] from sec-butyl bromide and sodium phenolate; b.p. 101-103° at 44 mm, $d^{20}_4$ 0.9346,

$n^{20}D$ 1.4945. 5 g of the substance in an ampule was cooled with solid carbon dioxide and saturated with dry HCl to an additional weight of 1 g. The ampule was sealed and heated in an autoclave with benzene for 6 hours to 250°. The mixture was treated as in the reaction of butylation of phenol. We obtained 1.25 g (25%) of a butylphenol fraction with b.p. 190-230° at 720 mm. From 0.8 g of this fraction by the process described above we obtained a mixture of butylphenoxyacetic acids: 0.2 g of crystals and 0.17 g of oil. The crystals after recrystallization from benzine melted at 112-113°, and were o-sec-butylphenoxyacetic acid (see Table 4).

Found %: C 69.29; H 7.75. $C_{12}H_{16}O_3$. Calculated %: C 69.20; H 7.74.

The p-toluidide of o-sec-butylphenoxyacetic acid melted at 70-71° (fine needles from aqueous alcohol).

Found %: C 76.68; H 7.78. $C_{19}H_{23}O_2N$. Calculated %: C 76.76; H 7.8.

## Free-Radical Butylation of Anisole

n-Butylphenyltriazene was prepared by the method of Dimroth [19]. Its m.p. was 20-21°, $n^{20}D$ 1.5719, silver salt melted at 101-104° [20, 21].

9.1 g of n-butylphenyltriazene in 30 g of anisole was gradually added to 20 g of anisole heated to 125° (apparatus filled with nitrogen). The reaction was ended after 5-6 hours, the temperature of the mixture was 140-145°. The main mass of anisole (47.3 g) was removed by distillation. The residue was treated with 15% HCl to remove bases. The neutral part was distilled in a fractionating column. The primary and secondary amines were separated by metaphosphoric acid [22]. The physical constants of the isolated substances and the melting points of their derivatives are given in Table 3.

Analysis of o-n-butylphenoxyacetic acid with m.p. 105-106° (needles from aqueous alcohol) gave the following results.

Found %: C 69.4; H 7.73. $C_{12}H_{16}O_3$. Calculated %: C 69.2; H 7.74.

The melting points of the butylphenoxyacetic acids and their toluidides, which were obtained from the different isomers of butylphenol, are given in Table 4. Mixed melting point of the o-n- and p-sec-butylphenoxyacetic acids gave a sharp depression.

## SUMMARY

1. We have studied the reaction of butylation of benzene, naphthalene, phenol, and anisole in the presence of copper. We have shown that at 200-250° alkylation products are formed in 38-87% yields. Thermal butylation also gives alkyl derivatives.

2. Under the given conditions, in all cases, there is isomerization of the primary butyl group to the secondary. Butylation of phenol goes by direct alkylation of the ring.

3. The free butyl radicals formed by thermal decomposition of n-butylphenyltriazene alkylate the anisole ring.

## LITERATURE CITED

[1] I. P. Tsukervanik and S. G. Mel'kanovitskaia, Zh. O. Kh. 27, 885 (1957);* I. P. Tsukervanik and G. S. Semeshko, Zh. O. Kh. 27, 1143 (1957).*

[2] G. F. Hennion and J. G. Anderson, J. Am. Chem. Soc. 68, 424 (1946).

[3] I. N. Nazarov, N. V. Kuznetsov, and A. V. Semenovskii, DAN SSSR 99, 1003 (1954).

[4] T. Estreicher, Ber. 33, 436 (1900).

[5] V. S. Johnson, R. D. Shannon and R. A. Rid, Organic Reagents for Organic Analysis, IL, 1948.**

[6] I. P. Tsukervanik and V. D. Tambartseva, Biull. SAGU, No. 22, 221 (1938).

[7] A. F. Bickel and E. C. Kooyman, Rec. trav. chim. 71, 1137 (1952).

---

*Original Russian pagination. See C.B. translation.

**Russian translation.

[8] M. Levy and M. Szwarc, J. Am. Chem. Soc. 77, 1949 (1955).

[9] A. L. J. Beckwith and W. A. Waters, J. Chem. Soc. 1957, 1665.

[10] A. V. Topchiev, Ia. M. Paushkin, and M. V. Kurashev, DAN SSSR 108, 95 (1956).

[11] Beilst. VI, 522.

[12] Dictionary of Organic Compounds I, 160 (1949).*

[13] R. A. Smith, J. Am. Chem. Soc. 55, 3713 (1933).

[14] Dictionary of Organic Compounds I, 360 (1949).*

[15] V. N. Ipatieff and L. Schmerling, J. Am. Chem. Soc. 59, 1056 (1937).

[16] A. Baeyer, Lieb. Ann. 245, 140 (1888).

[17] I. P. Tsukervanik and I.V. Terent'ev, Zh. O. Kh. 7, 637 (1937).

[18] W. A. Pardee and W. Weinrich, Ind. Eng. Chem. 36, 595 (1944).

[19] O. Dimroth, Ber. 38, 2328 (1905).

[20] B. A. Dolgoplosk, B. L. Erusalimskii, V. A. Krol', and L. M. Romanov, Zh. O. Kh. 24, 1775 (1954).**

[21] V. Ia. Pochinok and O. I. Shevchenko, Ukrain. Khim. Zh. 20, 289 (1954).

[22] W. Schlomann, Ber. 26, 1020 (1893).

[23] Dictionary of Organic Compounds I, 156 (1949).*

[24] Beilst. XII, 168.

[25] J. B. Niederl, V. Niederl, S. Shapiro and M. E. Greal, Ch. A. 31, 5337 (1937).

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*In Russian.

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# THE CONDENSATION OF BENZOTRICHLORIDE WITH BENZENE IN THE PRESENCE OF ALUMINUM CHLORIDE

I. P. Tsukervanik and Z. Ia. Belinson

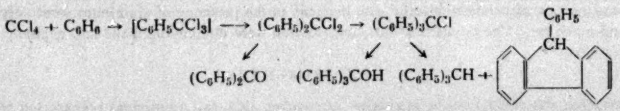
The alkylation of the aromatic ring by polyhalogen compounds is of interest for the explanation of the possibility of stepwise occurrence of the reaction and especially for the study of the conditions of formation of the anomalous products which are often found in this synthesis [1].

Doebner [2] and Schwarz [3] reported that they obtained only triphenylmethane from benzotrichloride and benzene. Ray [4], and then Wohl and Wertyporoch [5], changed the conditions of this reaction and isolated 9,9',10,10'-tetraphenylhydroanthracene.

Newman and Pinkus [6] studied the condensation of benzatrichloride with p-cresol and among other substances obtained 2-hydroxy-5-methylbenzophenone as a product of the hydrolysis of the intermediate dichloride. In one of the patents [7] there is a method for the synthesis of diarylketones based on the condensation of benzotrichloride with aromatic compounds.

In a number of works the reaction of carbon tetrachloride with benzene has been studied; the first intermediate product should be benzotrichloride. Friedel and Crafts [8], Boeseken [9], and Gomberg [10] showed the successive substitution of chlorine atoms of carbon tetrachloride: diphenyldichloromethane and triphenylchloromethane were formed. However, in no case were benzotrichloride and tetraphenylmethane obtained. Besides these substances, hydrolysis products were formed in the condensation of carbon tetrachloride: triphenylcarbinol and benzophenone, and also triphenylmethane and 9-phenylfluorene [11-13].

On the basis of the literature data we can give the following scheme for these condensations:


$CCl_4 + C_6H_6 \rightarrow [C_6H_5CCl_3] \longrightarrow (C_6H_5)_2CCl_2 \rightarrow (C_6H_5)_3CCl$
$(C_6H_5)_2CO$
$(C_6H_5)_3COH$
$(C_6H_5)_3CH \rightarrow$
$C_6H_5$
CH

We have studied the condensation of benzotrichloride with benzene in order to carry out the successive substitutions of chlorine atoms and to determine the conditions of formation of triphenylmethane and 9-phenylfluorene.

It was shown that a basic factor which determines the results of the synthesis is the amount of $AlCl_3$. With 0.1 g mole of $AlCl_3$ (per 1 g mole of benzotrichloride), independent of temperature (15-90°) and ratio of reagents, diphenyldichloromethane was obtained in yields to 70%, with small admixtures of triphenylchloromethane. With 1 g mole of $AlCl_3$, the chief product was triphenylchloromethane (80-85%). Further increase in the amount of $AlCl_3$ (to 2 g mole) caused accumulation of tars and the yield of triphenylchloromethane fell.

The experiments carried out by Wohl and Wertyporoch [6] (1.5 g moles $AlCl_3$) gave us only triphenyl carbinol which in melting point and external appearance is similar to the 9,9',10,10'-tetraphenyldihydroanthracene described by these authors. The authors gave no indication of the identification of this substance except the melting point.

Further, we studied the effect of different factors on the results of the condensation.

When the reaction complex was treated with an excess of weakly acid solution, besides the chlorides there was produced a considerable amount of the hydrolysis products: benzophenone and triphenyl carbinol. We avoided hydrolysis by pouring the reaction mixture into ice and concentrated hydrochloric acid.

It was long ago observed [2, 8, 10] that distillation of triphenylchloromethane at ordinary pressure (250-300°) caused its decomposition to triphenylmethane and phenylfluorene.

In our experiments we showed that freezing the benzene solution of the reaction mixture or its vacuum distillation gave triphenylchloromethane and triphenyl carbinol without admixture of triphenylmethane and 9-phenylfluorene. This latter substance actually accumulated in appreciable amounts after distillation of the crude reaction product at ordinary pressure.

We also studied the effect of ultraviolet illumination on the course of the triphenylchloromethane synthesis. In this connection we considered the data of Gomberg [14], Schmidlin [15], and Letsinger [16] on the conversion of of triphenylmethane in benzene solution in the light. They indicate the formation here of triphenylmethane, di-(9-phenylfluorenyl), and 9-phenylfluorene.

The condensation of benzotrichloride with benzene in ultraviolet light leads only to sharp increase in yield of triphenylchloromethane (98%). No other substance was isolated.

The effect of water in the $AlCl_3$ or the addition of water to the reaction mixture on the course of the alkylation is well known. In this case the addition of small amounts of water caused only a lowering in the yield of triphenylchloromethane (63%).

Reducing processes are often found in these alkylations in the presence of easily dehydrogenated hydrocarbons in the reaction mixture (dihydroanthracene, cyclohexane, etc.) [1]. Based on the work of Nenitzescu [17], we carried out the condensation of benzotrichloride with benzene to which was added (30%) cyclohexane. In this case we did not obtain one normal alkylation product. We isolated about equal amounts of diphenylmethane, triphenylmethane, and 9-phenylfluorene (60% in all). Such a result shows that even in the first stage of the reaction there is reduction of diphenylchloromethane. The idea of Norris [11] for the synthesis of triphenylmethane is based on another principle. The addition of ether to the complex of triphenylchloromethane with $AlCl_3$ leads to an ethyl ether of triphenyl carbinol which is split under the influence of $AlCl_3$ to triphenyl methane and acetaldehyde. In this case there is a combined hydrogenation—dehydrogenation which occurs intermolecularly and intramolecularly (9-phenylfluorene).

The replacement of $AlCl_3$ by metallic aluminum often also leads to reduction processes in condensations with polyhalogen compounds. For example, chloroform and benzene with aluminum give diphenylmethane and small yields of triphenylmethane [18, 19].

Our condensation of benzotrichloride with benzene in the presence of aluminum went very violently and always formed much tar. The products of this condensation were diphenylmethane and triphenylmethane.

## EXPERIMENTAL*

Condensation was carried out by gradually introducing $AlCl_3$ (a commercial preparation—GOST 4452-48) into a mixture of benzotrichloride and benzene. At the end of the reaction the mixture was decomposed with water, or with ice and concentrated hydrochloric acid. The benzene solution of the reaction product was dried and fractionated, or frozen after addition of ether.

We give typical examples of condensation in the table.

### Condensation of Benzotrichloride with Benzene in the Presence of Cyclohexane

To a solution of 9.8 g of benzotrichloride in 50 ml of benzene and 25 ml of cyclohexane was gradually added 6.7 g of $AlCl_3$. The mixture stood for 20 hours at 20° and then was heated for 2 hours at 70°. After decomposition by acidified water the benzene layer was washed, dried, and fractionated. We obtained 1.4 g (17%) of diphenylmethane, 2.6 g (21%) of triphenylmethane, and 2.6 g (21%) of 9-phenylfluorene.

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*Part of the experiments were run by T. Mametzhanov.

## Condensation in Ultraviolet Light

After adding 6.7 g of $AlCl_3$ in 75 ml of benzene to a solution of 9.8 g of benzotrichloride in a quartz flask, we illuminated the mixture for 3 hours with a PRK-2 lamp. Further illumination (2-3 hours) was repeated three times in alternation with heating on the water bath. Altogether, the illumination lasted 8 hours.

The reaction mixture was treated with ice and concentrated hydrochloric acid (50 g). The benzene layer was separated and fractionated. We obtained 13.7 g (98%) of trichloromethane.

## Condensation in the Presence of Aluminum

To a solution of 19.5 g of benzotrichloride in 40 ml of benzene was added 6.27 g (0.01 g atom) of fresh aluminum filings. The mixture was heated to weak boiling. After 5 minutes, darkening began and then the aluminum dissolved. Heating was stopped. An energetic reaction (much like a Grignard) at once went on without evolution of HCl. After a half hour, an oily lower layer formed, and intense evolution of HCl began. The mixture stood at 20° for 12 hours. After being washed with water, the benzene layer was distilled. We isolated: benzotrichloride 6.6 g (35%), diphenylmethane 3.8 g (16%), triphenylmethane 0.9 g (4%), tar 6 g.

In another similar experiment with double the amount of aluminum we obtained: diphenylmethane 21%, triphenylmethane 11%. The experiment carried out in a stream of nitrogen did not differ appreciably.

TABLE

| Molar ratio $C_6H_5CCl_3 : C_6H_6 : AlCl_3$ (experiment with 0.1 g mole of $C_6H_5CCl_3$) | Temperature | Duration (hours) | Yield of products (in %) | | | Notes |
|---|---|---|---|---|---|---|
| | | | Diphenyldichloromethane | Triphenylchloromethane | Triphenyl carbinol | |
| 1 : 4.5 : 0.1 | 20° | 24 | 36 | – | – | Recovery of benzotrichloride, 60% |
| 1 : 4.5 : 0.1 | 90 | 2 | 47 | 20 | – | |
| 1 : 17 : 1 | 20 | 20 | – | 75 | 8 | Decomposition by acidified water |
| 1 : 17 : 1 | 80 | 4 | – | – | 82 | |
| 1 : 2.5 : 1 | 80 | 4 | – | 88 | 5 | Decomposition by ice and HCl |
| 1 : 6 : 1.5 | 20 | 24 | – | – | 84 | Decomposition by acidified water |

Diphenyldichloromethane was isolated by fractionation of the mixture of products after removal of excess benzene.

B.p. 137-140° at 9 mm, $d^{20}_4$ 1.2339.

Freshly prepared diphenylchloromethane always had a bright blue color. When it stood in a closed flask it gradually lost the color and crystallized with simultaneous evolution of HCl. The crystals were benzophenone with m.p. 47.48°, oxime, m.p. 139-140°.

When diphenyldichloromethane was hydrolyzed by boiling it with water, it gave pure benzophenone.

Evidently the blue color of diphenyldichloromethane was connected with the start of the conversion to benzophenone which occurred through free ions or radicals.

Triphenylchloromethane was isolated by distillation (185-195° at 7 mm) or by freezing from a benzene-ether solution. When it was recrystallized from petroleum ether it melted at 108-109°. It was identified by mixed melting point with a known preparation.

Triphenyl carbinol was isolated from the mother liquors after crystallization of triphenylchloromethane. In some experiments it was the main product and was obtained by distillation. B. p. 178-180° at 2 mm. After crystallization from glacial acetic acid it melted at 159-160°. It gave no depression of melting point when mixed with a known preparation of triphenyl carbinol.

Diphenylmethane boiled at 130-132° at 15 mm. It crystallized when cooled. For identification we obtained 4,4'-dinitrodiphenylmethane with m.p. 184° [20].

Triphenylmethane was obtained by fractionation of the mixture of crude products which boiled at 175-180° at 5 mm. After it was recrystallized from acetic acid it melted at 91-92°. It was identical with a known preparation of triphenylmethane.

9-Phenylfluorene was isolated by distillation along with triphenylmethane. It was separated by fractional crystallization from acetic acid (isolated from the mother liquors), m.p. 145-146°.

For identification we compared it with a preparation synthesized from triphenylcarbinol by distillation with phosphoric acid [21]. The mixed melting point of both preparations gave no depression.

## SUMMARY

1. We have showed that the condensation of benzotrichloride with benzene goes by successive replacement of one or two atoms of chlorine depending on the amount of $AlCl_3$. With 0.1 g mole $AlCl_3$, diphenyldichloromethane is formed; with 1 g mole $AlCl_3$, triphenylchloromethane is obtained in yields up to 98%.

2. The products of reduction and dehydrogenation (diphenylmethane, triphenylmethane, phenylfluorene) do not occur under ordinary conditions of the condensation. These anomalous products occur in the presence of cyclohexane or when metallic aluminum is used as the catalyst.

## LITERATURE CITED

[1] I. P. Tsukervanik, Studies in the Field of Alkylation of the Aromatic Ring Compounds, Tr. SAGU, No. 71, 70 (1955).

[2] A. Doebner, Ber., 12, 1462 (1879).

[3] H. Schwarz, Ber., 14, 1516 (1881).

[4] I. N. Ray, Zbl., 1921, I, 369.

[5] A. Wohl and E. Wertyporoch, Lieb. Ann., 481, 30 (1930).

[6] M. Newman and A. Pinkus, J. Org. Ch., 19, 985 (1954).

[7] H. Seifert and B. Wenk, R. Zh. Khim., 1956, 44480.

[8] C. Friedel and J. Crafts, Ann. Chim., 1, 449 (1884); Bull. Soc. Chim., 36, 1 (1881).

[9] J. Boeseken, Zbl., 1905, I, 1248.

[10] M. Gomberg, Ber., 33, 3144 (1900).

[11] I. Norris and R. Young, J. Am. Chem. Soc., 46, 2580 (1924).

[12] Synthetic Organic Preparations I, 423 (1952).*

[13] E. and O. Fischer, Lieb. Ann. 194, 257 (1878).

[14] M. Gomberg, Ber., 37, 3538 (1904).

[15] I. Schmidlin and A. Garsia-Banus, Ber., 45, 1344 (1912).

[16] K. Letsinger, K. Collat and M. Magnuson, J. Am. Chem. Soc. 76, 4185 (1954).

[17] C. Nenitzerscu and C. Ionescu, Lieb. Ann., 491, 189 (1931).

[18] B. N. Dolgov and I. N. Kuchumova, Zh. O. Kh. 21, 509 (1951).**

---

*In Russian.

**Original Russian pagination. See C.B. translation.

[19] K. I. Porshakova, N. G. Sidorova, and I. P. Tsukervanik, Zh. O. K. 26, 1375 (1956).*

[20] Beilst.,V, 595.

[21] Beilst., V, 721.

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# A STUDY OF THE MOBILITY OF THE ETHYL GROUP IN ETHYLBENZENE AND ITS DERIVATIVES BY THE METHOD OF ISOTOPE EXCHANGE

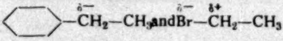
L. M. Nazarova

In a previous work [1] it was shown that the tertiary butyl group in tert-butylbenzene partially exchanged with the tert-butyl group in tert-butyl chloride at 120° in the presence of $FeCl_3$ and $AlCl_3$ and in the case of tert-butylphenol, such an exchange occurred without a catalyst.

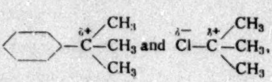
In the present work we have studied the exchange of the ethyl group between ethylbenzene, its nitro derivatives (o-, m-, and p-) and ethylphenols (o-, m-, and p-) on the one hand, and ethyl bromide on the other. We have also studied the exchange between ethylbenzene and metal ethyls (−Na, −MgBr, −Zn−) and for comparison, between tert-butylbenzene and metal ethyls (−Na, −MgBr).

On the basis of the work of Anschutz [2] and Heise and Töhl [3] which established the mobility of the ethyl group in ethylbenzene when it was boiled with aluminum chloride, and the Friedel-Crafts reaction which showed the mobility of the ethyl group in ethyl bromide, we could expect that exchange of groups between ethylbenzene and ethyl bromide in the presence of aluminum chloride should occur. However, our experiments showed that in this case there was no exchange; only the Friedel-Crafts reaction occurred. In the case of ethyl phenols also there was only substitution; while with tert-butylbenzene and tert-butylphenols the substitution and exchange reactions went on simultaneously [1].

This led us to the assumption that the absence of exchange in the case of ethylbenzene and ethyl bromide probably depended on the different δ-charges on the carbon of the ethyl group in ethylbenzene and in ethyl bromide, namely:



while in tert-butylbenzene and tert-butyl chloride the charges on the tertiary carbon atom of the butyl group were the same:



and in this case, exchange was found.

To test this idea we ran a series of experiments on the exchange of the ethyl group between ethylbenzene and metal ethyls, where we could expect negative charges on the carbon of the ethyl group bound to the metal.

In the Table we give the results of these experiments. From this table it can be seen that actually ethylbenzene and diethylbenzene exchange with metal ethyls which tend to split ionically ($C_2H_5Na$, $C_2H_5MgBr$). There is no exchange with diethyl zinc.

At the same time experiments showed that the tertiary butyl group in tert-butylbenzene did not exchange at all with the ethyl group.

TABLE

Exchange Between Metal Ethyls and Ethylbenzene, Diethylbenzene, and Tert-Butylbenzene

| No. | System | Experimental conditions | Activity of second component in $\mu$ Cu/mole | | Exchange (in %) |
|---|---|---|---|---|---|
| | | | starting | after the experiment | |
| 1 | $CH_3CH_2MgBr + C_2H_5 \cdot C_6H_5$ (ether solution) | A mixture of freshly prepared labeled ethylmagnesium bromide (in ether) with ethylbenzene at room temperature, 2 weeks. | 0 | 0 | None |
| 2 | The same | The same mixture heated at 150° for 20 hours. | 0 | 1.5 | 1.6 |
| 3 | The same | The magnesium organic compound was obtained in the presence of ethylbenzene. | 0 | 5.3 | 5.6 |
| 4 | $C_2H_5MgI + (CH_3)_3C \cdot C_6H_5$ | The magnesium organic compound was obtained in the presence of labeled tert-butylbenzene. | 630 | 630 | None |
| 5 | $(C_2H_5)_2Zn + (C_2H_5)_2C_6H_4$ (labeled in the ethyl group) | 150°, 5 hours | 125 | 123 | None |
| 6 | $C_2H_5Na + (C_2H_5)_2C_6H_4$ (labeled in the ethyl group) | The same | 125 | 77 | 76.8 |
| 7 | $C_2H_5Na +$<br>$+ (CH_3)_3C \cdot C_6H_5$ | The same | 630 | 632 | None |

These facts confirm our assumption that in the ionic type of exchange, the exchanging groups which have the same sign of $\delta$-charge on the carbon atoms will exchange.

## EXPERIMENTAL

Ethyl bromide labeled with $C^{14}$ was obtained from labeled ethyl alcohol by the action of phosphorus pentabromide. Before ending the distillation of ethyl bromide, nitrogen was blown through the apparatus. The reaction product was removed in a trap cooled with dry ice, washed with ice water, and dried over calcium chloride.

The yield of ethyl bromide based on the alcohol was 65%. Analysis of the activity was carried out as described earlier [1]. The activity of the preparation was 192.6 $\mu$ Cu/mole (counted with an accuracy of 1%).

Diethylbenzene labeled with $C^{14}$ in the ethyl group was synthesized in a manner analogous to the labeled tert-butylbenzene [1]. From the mixture of mono-, di-, and triethylbenzenes obtained in the synthesis, we isolated a p-diethylbenzene fraction (b.p. 180-185°) with an activity of 125 $\mu$Cu/mole (accuracy of counting 1.2%).

Ethyl sodium was synthesized by the method of Gilman and Young [4]. o- and p-Nitroethylbenzenes were obtained by ordinary nitration of ethylbenzene. They were separated by repeated distillation in a vacuum. Separation was controlled by determination of refraction.

m-Nitroethylbenzene was prepared by the method of Hodgson and Walker [5], by diazotizing p-amino-m-nitroethylbenzene with elimination of the diazo group.

o-, p-, and m-Ethylphenols were obtained from the corresponding nitro compounds through the amino and diazo compounds.

The constants of the substances which we synthesized corresponded to those given in the literature.

## Exchange Between Ethylbenzene or its Derivatives and Labeled Ethyl Bromide

An equimolecular mixture of the substance* (0.01 mole) was sealed in a glass ampule which was then heated in an air thermostat at 150 ± 2° for 30 hours. At the end of the experiment, the ethyl bromide was distilled off directly from the ampule and redistilled twice, after which the activity was determined.

In all cases the activity remained unchanged.

## Exchange of Ethylbenzene with Metal Ethyls

The exchange was carried out in glass ampules blown out with dry nitrogen. The substances, in approximately equimolecular amounts, were placed in the ampule under nitrogen and the ampule was sealed under nitrogen.

The Grignard reagent was prepared in the usual way with the following amounts: 0.6-1 g magnesium, 2.5-4.3 g ethyl bromide, 20 ml of dry ether. Before placing the Grignard reagent in the ampule, about half the ether was removed by passing nitrogen through it.

Ethyl sodium was placed in the ampule in benzene suspension. In the ampule it was washed 5-6 times with petroleum ether and dried in a stream of nitrogen.

When heating was finished, the ampule was opened under nitrogen and joined to an apparatus which permitted us to carry out decomposition of the organometallic compound in a stream of nitrogen, after which the second component of the mixture was removed by petroleum ether and dried over calcium chloride. After distillation of the petroleum ether, the residue was distilled in a vacuum and analyzed for activity.

In the experiments with tert-butylbenzene, run for comparison, the evidence for activity (if exchange had occurred) could be expected in the first drops of the distillate (because of the effect of admixtures of ethylbenzene), and so the first fractions of the vacuum distillate were analyzed.

The count was made with an accuracy of 1-2%. The conditions of the experiment and the results are given in the Table.

We express thanks to N. I. Sheverdina for the preparation of diethyl zinc.

## SUMMARY

1. We have found that at 150° ethylbenzene, nitroethylbenzene (o-, m-, and p-) and ethylphenol (o-, m-, and p-) do not exchange ethyl groups with ethyl bromide which is labeled with $C^{14}$. In the case of ethylbenzene and ethylphenol, only substitution occurs.

2. We have expressed the opinion that this absence of exchange in distinction to tert-butylbenzene and its derivatives depends on the different $\delta$-charges on the carbon atom of the substituting group; in an ionic type of exchange, the exchanging groups should have the same sign of $\delta$-charge on the carbon atoms.

3. Ethylbenzene (or paradiethylbenzene) enters an exchange reaction with metal ethyls which tend to undergo ionic splitting ($C_2H_5MgBr$, $C_2H_5Na$).

In distinction to ethylbenzene, tert-butylbenzene does not exchange its side chain group in the reaction with ethylmagnesium bromide or sodium ethyl.

These facts confirm the idea of the role of the $\delta$-charge on the carbon atom of the exchanging groups.

## LITERATURE CITED

[1] L. M. Nazarova, J. Gen. Chem. 26, 1640 (1956).**

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*In the case of ethylbenzene and its derivatives we added a catalyst ($AlCl_3$ or $FeCl_3$) in amount 0.01 g.

**Original Russian pagination. See C.B. translation.

[2] R. Anschütz, Lieb. Ann. 235, 189 (1886).

[3] R. Heise, and A. Töhl, Lieb. Ann. 270, 159 (1892).

[4] H. Gilman and R. V. Young, J. Org. Ch. 1, 326 (1936).

[5] H. H. Hodgson, and J. Walker, J. Chem. Soc. 1933, 1620.

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# THE SYNTHESIS OF SOME NITRO- AND AMINO DERIVATIVES OF TOLAN

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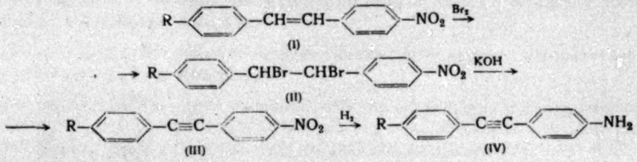
For certain studies which were carried out in our laboratory we needed 4-aminotolan (4-aminodiphenylacetylene) and its corresponding 4'-nitro derivative. Neither substance was described in the literature, and we adopted the following general scheme for their synthesis (R = H or $NO_2$):



The intermediate 4-nitrotolan of this scheme was also previously unknown.

It was particularly intersting in this preparation to note that, among the many products which we tried for the reduction of III ($Na_2S_2$, $(NH_4)_2S$, $H_2S$ in pyridine solution, hydrazine hydrate in the presence of Raney nickel, and others), the only positive results were obtained with phenylhydrazine, as recommended by Ruggli [1] for the partial reduction of 2,2'-dinitrotolan.

We showed the presence of a triple bond in substances III and IV as follows: 4-aminotolan was deaminated to give tolan, identical with the hydrocarbon prepared by known methods, and 4-amino-4'-nitrotolan was further reduced easily to the known 4,4'-diaminotolan.

## EXPERIMENTAL*

### Synthesis of 4-Aminotolan

Trans-4-nitrostilbene** (I, R = H) was synthesized by the method described in the literature [3] from diazotized p-nitroaniline and styrene in the presence of copper chloride, with only this difference, that the crude product was not purified by fractionation in a vacuum, but by steam distillation (145-175°) and later crystallization from normal butyl alcohol.

4-Nitrostilbene dibromide (II, R = H) was synthesized by the method of Pfeiffer and Sergiewskaja [4] with some additions and improvements by us.

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* Students E. G. Bratash, N. A. Vainshtein, and A. P. Pugina shared in the experimental part of the work.

** According to the data of Bergmann and Hervey [2], trans-4-nitrostilbene with m.p. 157° is easily obtained by reducing 4-nitrostilbene oxide, which in its turn is prepared from p-nitrobenzyl chloride by boiling it with benzaldehyde in the presence of potash. We carried out this synthesis and isolated a product which had all the properties claimed for it by these authors. However, attempts to obtain from it the described 4-aminostilbene [4] did not succeed, nor could the compound be converted to the known 4-nitrostilbene dibromide. We also showed that a mixed melting point of the compound of Bergmann and Hervey with the 4-nitrostilbene of whose authenticity there was no doubt [4] gave a sharp depression. Thus, we have established that the method of Bergmann and Hervey gives, not 4-nitrostilbene, but some other substance.

To a solution of 5.4 g of 4-nitrostilbene in 130 ml of chloroform was added 3 ml of bromine and the mixture was allowed to stand 3 hours at room temperature. Then the solvent was completely distilled off and the crystalline residue was recrystallized from toluene (with activated charcoal). Yield 9 g (97%); m.p. 195-197°

**4-Nitrotolan (III, R = H).** 3 g of 4-nitrostilbene dibromide was suspended in 150 ml of boiling methanol and a solution of 3 g of KOH in 30 ml of methanol was added dropwise through the reflux condenser over 30 minutes. The solid substance then quickly dissolved. When all the alkali had been added, the solution was boiled under reflux for another 30 minutes and the solvent was evaporated as completely as possible; otherwise the yield of reaction product often fell sharply. The crystalline residue was carefully ground with water, the crystals were separated from the liquid, washed, and boiled with a small amount of methyl alcohol. After they were cooled, they were filtered and recrystallized from normal butyl alcohol with activated charchoal. Yield, 1.6 g (92%); m.p. 202-203°.

4-Nitrotolan was a well-crystallized light-yellow substance, not soluble in water, difficultly soluble in methyl alcohol, and moderately soluble in isopropyl and butyl alcohols.

Found %: N 6.43, 6.18. $C_{14}H_9O_2N$. Calculated %: N 6.26.

**4-Aminotolan (IV, R = H).** A mixture of 0.45 g of 4-nitrotolan and 2.7 ml of phenylhydrazine was gradually heated on a paraffin bath with periodic shaking, in a vessel with an air reflux condenser (thermometer in bath). At about 120-130° everything dissolved and nitrogen began to be evolved. As the evolution of nitrogen became slower, the bath temperature was slowly raised and reaction again become lively.* Thus, the temperature was raised to 205-210°, where the mixture was kept for 20-30 minutes, after which evolution of nitrogen had practically stopped. The total time of heating was about 3 hours. The solution stood until the next day, and no crystals were seen in it, so that reduction was sufficiently complete. The solution was then carefully mixed with 135 ml of 5% sulfuric acid and the unreacted phenylhydrazine dissolved while the reaction product precipitated as a sulfate. The salt was filtered and washed with water, ethyl alcohol, and ether until the last portion of each wash solution was colorless. Yield 0.45 g (92%). To obtain the free base, we ground the amine sulfate with a cold solution of aqueous ammonia (1 : 1), washed the product with water, and recrystallized it from aqueous methyl alcohol (1 : 2). M.p. 126-127°.

4-Aminotolan was a white, crystalline substance, insoluble in water and easily soluble in ordinary organic solvents.

Found %: $NH_2$** 8.13, 8.24. $C_{14}H_{11}N$. Calculated %: $NH_2$ 8.29.

**Deamination of 4-aminotolan.** To a solution of 0.1 g of 4-aminotolan in 3 ml of glacial acetic acid we added 0.6 ml of concentrated hydrochloric acid, and cooled the crystallizing mixture to 0°; to this, gradually and with good stirring, we added a solution of 0.036 g of sodium nitrite in 0.5 ml of water. The resulting diazo solution was filtered and slowly added to a cooled mixture of 1 g of potassium hypophosphite and 2 ml of hydrochloric acid (1 : 1), and it was all stirred. The solution stood for several hours in ice, and then over night at room temperature. The precipitate was separated from the liquid and the reaction product was extracted from it with boiling ethyl alcohol; the solution was treated with activated charcoal, evaporated to small volume and the reaction product was carefully precipitated by the addition of water. Yield 0.06 g (65%). After recrystallization from aqueous ethyl acohol, white crystals with m.p. 60-61°. A mixed melting point of these crystals with a known sample of tolan [6] gave no depression.

### Synthesis of 4-Amino-4'-nitrotolan

**4,4'-Dinitrostilbene (I, R = $NO_2$).** The substance was obtained by the action of alcoholic alkali on p-nitrobenzylchloride by the method of Walden and Kernbaum [7]. This gave a mixture of isomers (cis and trans), which, as we have found, need not be carefully separated in this case, and immediately after the reaction it is enough to recrystallize them once from nitrobenzene or pyridine. The product with m.p. 275-280° consists chiefly of the trans-isomer and was used for further reactions.

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* The course of the reaction was satisfactorily controlled by following the intensity of evolution of bubbles of gas in a glass capillary joined by a rubber tube to the upper part of the condenser and leading from the other end to a vessel which contained about 0.5 ml of water.

** The description of a micromethod for determination of aromatic amino groups can be found in a previously published paper [5].

4,4'-Dinitrostilbene dibromide (II, R = $NO_2$). 7 g of 4,4'-dinitrostilbene was suspended in 280 ml of glacial acetic acid, heated to 50-60°, and then over 5-10 minutes 3.6 ml of bromine was added with continuous shaking. The mixture was heated to boiling and kept at this temperature for 1.5-2 hours, with periodic shaking. Part of the precipitate dissolved. Without filtering, about two thirds of the solvent was distilled off. The remaining liquid was cooled and allowed to stand for some time for more complete precipitation of the reaction product. The crystals were filtered and washed with a small amount of warm acetone. Yield 10.1 g (91%). This substance with m.p. 265-270° was used without further purification in the next step of the synthesis.

The use of dioxane as a solvent in this reaction, as recently recommended [8], according to our results gives a product of poor quality.

4,4'-Dinitrotolan (III, R = $NO_2$) was obtained as described in the literature [8] and was recrystallized from glacial acetic acid. Yield 65-70%, m.p. 214°

4-Amino-4'-nitrotolan (III, R = $NO_2$). 3 g of 4,4'-dinitrotolan, 3.5 ml of phenylhydrazine, and 30 ml of m-xylene were slowly heated with periodic shaking in a large vessel with a reflux condenser, deeply immersed in a paraffin bath. When the temperature reached 115-120°, a weak evolution of nitrogen began (control of the reaction was carried out here in the same way as in the synthesis of 4-aminotolan). At 135-140° the substance began to dissolve; solution soon was complete and evolution of nitrogen became stronger. Then the bath temperature was raised to 145-150° in such a way that the reaction did not become too violent, and it was kept at this level for 3 hours. At the end of this time, evolution of nitrogen had almost completely stopped and the solution had become orange-red. The mixture was cooled and allowed to stand until the next day. The red needles which precipitated were filtered (2.7 g) and dissolved in 90 ml of hot chlorobenzene. A stream of dry hydrogen chloride was passed into the still-warm solution (50-60°) until the amine hydrochloride had precipitated completely in the form of light-yellow crystals. The precipitate was ground with a cold solution of aqueous ammonia and then washed with water. Yield 2.4 g (90%); m.p. 195°. For more complete purification the product was recrystallized from chlorobenzene (activated charcoal), and the melting point was thus raised to 198-200°

4-Amino-4-nitrotolan is an intensely red substance, easily soluble in nitrobenzene and pyridine, moderately soluble in glacial acetic acid, xylene, and chlorobenzene, and soluble with difficulty in alcohol; insoluble in water.

Found %: $NH_2$ 6.66, 6.59. $C_{14}H_{10}O_2N_2$. Calculated %: $NH_2$ 6.73.

Reduction of 4-amino-4'-nitrotolan to 4,4'-diaminotolan was carried out with zinc dust in hydrochloric acid under conditions analogous to those under which 4,4'-diaminotolan was obtained from 4,4'-dinitrotolan [8, 9]. When we carried out parallel experiments on the reduction of 4-amino-4'-nitrotolan and 4,4'-dinitrotolan we found that the reaction with the first substance went much more smoothly and with better yield. In both cases we obtained absolutely identical 4,4'-diaminotolan. From these, by diazotization and coupling of the diazo compound with H acid in an alkaline medium (performed by B. M. Krasovitskii), we synthesized the same azo dye, identical in all properties including the absorption spectrum.

## SUMMARY

We have synthesized the undescribed 4-nitrotolan, 4-aminotolan, and 4-amino-4'-nitrotolan.

## LITERATURE CITED

[1] P. Ruggli, Lieb. Ann. 412, 8 (1917).

[2] E. Bergmann and J. Hervey, Ber. 62, 905 (1929).

[3] W. Brunner and J. Kustatscher, Monatsh. 82, 100 (1951).

[4] P. Pfeiffer, and S. Sergiewskaja, Ber. 44, 1107 (1911).

[5] L. M. Litvinenko and A. P. Grekov, J. Anal. Chem. 10, 164 (1955) [See C.B. translation].

[6] Synthetic Organic Preparations, 3, 231 (1952)[in Russian].

[7] P. Walden and A. Kernbaum, Ber. 23, 1959 (1890).

[8] R. Belcher, M.Kapel and A. Nutten, Anal. Chim. Acta 8, 122 (1953).

[9] H. Reinhardt, Ber. 46, 3598 (1913).

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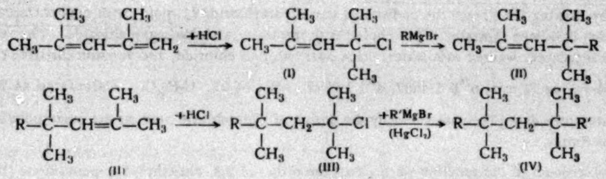
# THE SYNTHESIS OF HYDROCARBONS

## LXV. DI-TERT-ALKYLMETHANES FROM 2,4-DIMETHYL-1,3-PENTADIENE

R. Ia. Levina, Iu. S. Shabarov, and V. K. Daukshas

In a previous communication we described [1] the preparation of alkanes with two quaternary carbon atoms separated by a $CH_2$ group (di-tert-alkylmethanes); they were synthesized by reaction of alkylmagnesium bromides (in the presence of mercuric chloride) with tertiary chlorides (III) which already contained one quaternary carbon atom. The starting tertiary chlorides of structure III were obtained in 90% yields from the hydrochlorides of the corresponding ethylenic hydrocarbons with quaternary carbon atoms (II), which in turn were synthesized in 45-65% yields by the action of 2,4-dimethyl-1,3-pentadiene hydrochlorides* on alkylmagnesium bromides. Thus, in our method for the synthesis of di-tert-alkylmethanes the starting substance was actually 2,4-dimethyl-1,3-pentadiene; the synthesis was carried out as follows:



$$CH_3-\overset{CH_3}{\overset{|}{C}}=CH-\overset{CH_3}{\overset{|}{C}}=CH_2 \xrightarrow{+HCl} CH_3-\overset{CH_3}{\overset{|}{C}}=CH-\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-Cl \ (I) \xrightarrow{RMgBr} CH_3-\overset{CH_3}{\overset{|}{C}}=CH-\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-R \ (II)$$

$$R-\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-CH=\overset{CH_3}{\overset{|}{C}}-CH_3 \ (II) \xrightarrow{+HCl} R-\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-CH_2-\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-Cl \ (III) \xrightarrow[(HgCl_2)]{+R'MgBr} R-\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-CH_2-\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-R' \ (IV)$$

In the work cited above [1] we synthesized symmetrical di-tert-alkylmethanes of the general formula IV which contained only radicals with a normal structure (where $R = R' = CH_3$; $C_2H_5$; $n\text{-}C_3H_7$; $n\text{-}C_4H_9$). In the present work we have used the same method to obtain other previously undescribed alkanes IV which also have a symmetrical structure, but more branching (where $R = R' = iso\text{-}C_3H_7$; $iso\text{-}C_4H_9$; $iso\text{-}C_5H_{11}$; $-CH(CH_3)C_2H_5$; $CH(CH_3)C_3H_7$; we also synthesized some unsymmetrical di-tert-alkylmethanes (where $R = CH_3$ and $R' = C_3H_7$; $R = iso\text{-}C_3H_7$ and $R' = C_3H_7$; $R = CH(C_2H_5)_2$ and $R' = iso\text{-}C_3H_7$).

When we compare the constants of the alkanes with different structures synthesized in this and the previous [1] work, we can establish some regularities in the changes of the densities and coefficients of light refraction. Thus, the greatest densities and coefficients of light refraction are found in the most branched alkanes which contain the maximum number of quaternary and tertiary carbon atoms, especially when the quaternary and tertiary carbon atoms are found in a series (see Table 3). In the reaction with organomagnesium compounds the saturated tertiary chlorides (III) undergo not only exchange of a chlorine atom with the radical of the organomagnesium compound, but also loss of hydrogen chloride with the formation of the starting alkene (II) (50%) which can again be used for the synthesis of the alkanes IV. The yield of di-tert-alkylmethanes varied from 3 to 20% calculated on the tertiary chloride which reacted, and from 6 to 40% on that used.

It is important to note that di-tert-alkanes of this structure (IV) can also be obtained in several other ways:

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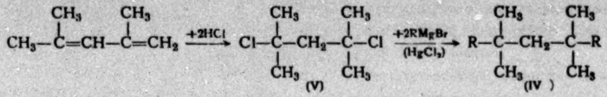
* In previous studies [2-5] we used the hydrobromides rather than the hydrochlorides of 2,4-dimethyl-1,3-pentadiene; the yield of alkenes was only 25-30%.

by exhaustive hydrochlorination of 2,4-dimethyl-1,3-pentadiene and reacting the thus prepared (in 65% yield) saturated ditertiary dichloride with a magnesium organic compound in the presence of mercuric chloride.



$$CH_3-\overset{CH_3}{\overset{|}{C}}=CH-\overset{CH_3}{\overset{|}{C}}=CH_2 \xrightarrow{+2HCl} \underset{(V)}{Cl-\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-CH_2-\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-Cl} \xrightarrow[(HgCl_2)]{+2RMgBr} \underset{(IV)}{R-\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-CH_2-\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-R}$$

By this reaction we synthesized one of the alkanes ($R = R' = C_2H_5$) in 5% yield, based on the starting dichloride, or ~ 3% based on the 2,4-dimethyl-1,3-pentadiene; during this reaction there is splitting of hydrogen chloride from the dichloride with formation of the starting diene and with its further dimerization.

Thus, this second method of synthesis gives a lower yield of di-tert-alkylmethane (IV) than the one considered above (the yield of the same hydrocarbon by the first method of synthesis, based on the 2,4-dimethyl-1,3-pentadiene, was 9%); also this permits the synthesis only of alkanes with a symmetrical structure ($R = R'$).

## EXPERIMENTAL

2-Chloro-2,4-dimethyl-3-pentene (I). 2,4-Dimethyl-1,3-pentadiene (b.p. 92-93° at 745 mm, $n^{20}D$ 1.4445, $d^{20}_4$ 0.7375; literature data [2]: b.p. 93-94° at 755 mm, $n^{20}D$ 1.4448, $d^{20}_4$ 0.7375) was treated with hydrogen chloride under the conditions described earlier [1, 6]. When the monohydrochloride was distilled or kept, hydrogen chloride split out, and so in the further reaction with RMgBr the dried, but not distilled, monohydrochloride was used immediately after it was obtained.

2,4-Dichloro-2,4-dimethylpentane (V). Exhaustive hydrochlorination of 2,4-dimethyl-1,3-pentadiene was carried out by shaking for 2 hours the undistilled monohydrochloride (1 mole) with concentrated hydrochloric acid (300 ml) which had been saturated, while cooled with ice water, with hydrogen chloride. The resulting dihydrochloride was separated, washed with water, dried over calcium chloride, and vacuum distilled (yield 104 g, 65%).

B.p. 60-62° at 11 mm, $n^{20}D$ 1.4537, $d^{20}_4$ 1.0292, $MR_D$ 44.51. $C_7H_{14}Cl_2$. Calculated 44.27.

The literature data [7] (synthesized by the action of hydrochloric acid on the corresponding glycol), b.p. 51.5-51.7° at 8 mm.

As a by-product of the reaction we isolated the dimer of 2,4-dimethyl-1,3-pentadiene (b.p. 90° at 10 mm, $n^{20}D$ 1.4800; literature data [3]: b.p. 91.5° at 11.5 mm, $n^{20}D$ 1.4797) and also the undescribed monohydrochloride of this dimer with m.p. 95° (from alcohol).

Found %: C 73.03; 71.83; H 11.15, 10.96; Cl 15.80, 15.71. $C_{14}H_{25}Cl$. Calculated %: C 73.48; H 11.02; Cl 15.50.

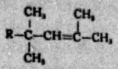
The same monhydrochloride with m.p. 95° was obtained by shaking the dimer of 2,4-dimethyl-1,3-pentadiene with hydrochloric acid saturated with hydrogen chloride; a mixed melting point of both preparations gave no depression.

Reaction of 2-chloro-2,4-dimethyl-3-pentene with alkylmagnesium bromides. 2-Chloro-2,4-dimethyl-3-pentene was reacted with primary alkyl ($R = CH_3$, iso-$C_4H_9$, and iso-$C_5H_{11}$) and secondary alkylmagnesium bromides ($R =$ iso-$C_3H_7$, sec-$C_4H_9$, and both isomers of sec-$C_5H_{11}$). The reaction was carried out under the conditions described earlier [1, 6]. The constants and yields of the alkanes (III) which were synthesized are given in Table 1. In all the experiments, the dimer of 2,4-dimethyl-1,3-pentadiene with b.p. 90° at 10 mm was isolated from the higher boiling fraction. The position of the double bond in the alkanes II was confirmed by ozonizing one of them, 2,4,4-trimethyl-5-ethyl-2-heptene ($R = CH(C_2H_5)_2$ ).

After decomposition of the ozonide by water, the latter was oxidized with hydrogen peroxide and soda was added to an alkaline reaction; the peroxide of acetone was steam-distilled from the mixture, m.p. 131-132°, (literature data [8] m.p. 132-133°); from the alkaline solution after the usual treatment was separated an acid with b.p. 237-238° at 750 mm, whose molecular weight corresponds to that of α,α-dimethyl-β-ethylvaleric acid (not described in the literature).

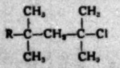
Found: M 159 (by titration). $C_9H_{18}O_2$. Calculated: M 158.2.

## TABLE 1

Alkenes of the General Structure 
$R{-}C(CH_3)_2{-}CH{=}C(CH_3){-}CH_3$

| R | Name | B. point pressure (mm) | $n_D^{20}$ | $d_4^{20}$ | Yield (in %) |
|---|---|---|---|---|---|
| $CH_3$ | 2,4,4-Trimethyl-2-pentene | 102—103° (740) | 1.4131 | 0.7183 | 65 |
| iso -$C_3H_7$ | 2,3,3,5-Tetramethyl-4-hexene | 152—153 (745) | 1.4382 | 0.7680 | 50 |
| iso-$C_4H_9$ | 2,4,4,6-Tetramethyl-2-heptene | 61—62 (20) | 1.4347 | 0.7608 | 53 |
| sec.-$C_4H_9$ | 2,4,4,5-Tetramethyl-2-heptene | 173.0—173.4 (742) | 1.4439 | 0.7825 | 48 |
| iso-$C_5H_{11}$ | 2,4,4,7-Tetramethyl-2-octene | 65—66 (11) | 1.4379 | 0.7690 | 55 |
| $C_3H_7{-}CH(CH_3){-}$ | 2,4,4,5-Tetramethyl-2-octene | 188.2—188.7 (750) | 1.4431 | 0.7820 | 46 |
| $C_2H_5{-}CH(C_2H_5){-}$ | 2,4,4-Trimethyl-5-ethyl-2-heptene | 192.0—192.5 (745) | 1.4461 | 0.7878 | 45 |

## TABLE 2

Tertiary Chlorides with the General Structure 
$R{-}C(CH_3)_2{-}CH_2{-}C(CH_3)_2{-}Cl$

| R | Name | Boiling point (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ found | $MR_D$ calc. |
|---|---|---|---|---|---|---|
| $CH_3$ | 2-Chloro-2,4,4-trimethylpentane* | 40—40.5° (12) | 1.4308 | 0.8746 | 44.01 | 44.01 |
| iso -$C_3H_7$ | 2-Chloro-2,4,4,5-tetramethylhexane | 65—66 (9) | 1.4498 | 0.8951 | 53.07 | 53.25 |
| iso -$C_4H_9$ | 2-Chloro-2,4,4,6-tetramethylheptane | 67- 68.5 (5) | 1.4464 | 0.8790 | 57.89 | 57.85 |
| sec -$C_4H_9$ | 2-Chloro-2,4,4,5-tetramethylheptane | 81—82 (10) | 1.4539 | 0.8937 | 57.84 | 57.86 |
| iso-$C_5H_{11}$ | 2-Chloro-2,4,4,7-tetramethyloctane** | 71—72 (1.5) | 1.4477 | 0.8789 | 62.35 | 62.48 |
| $C_3H_7{-}CH(CH_3){-}$ | 2-Chloro-2,4,4,5-tetramethyloctane | 62—63 (3) | 1.4516 | 0.8854 | 62.41 | 62.48 |
| $C_2H_5{-}CH(C_2H_5){-}$ | 2-Chloro-2,4,4-trimethyl-5-ethylpentane | 57—58 (2.5) | 1.4549 | 0.8908 | 62.36 | 62.48 |

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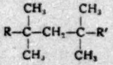
*Literature data [9]: b.p. 53° (29 mm), $n^{20}D$ 1.431.

** Found %: C 70.63, 70.60; H. 11.84; 12.02. $C_{12}H_{25}Cl$. Calculated %: C 70.36; H. 12.31.

TABLE 3

Di-tert-alkylmethanes 

$$R-\underset{CH_3}{\overset{CH_3}{C}}-CH_2-\underset{CH_3}{\overset{CH_3}{C}}-R'$$

| No. | Empirical formula | R | R' | Name | Boiling point (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ |  |  | Found % |  | Calc. % |  | Yield % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  |  |  | found | calc.* | calc. | C | H | C | H |  |
| 1 | $C_{11}H_{24}$ | $CH_3$ | $C_3H_7$ | 2,2,4,4-Tetramethylheptane | 58—58.5° (14) | 1.4232 | 0.7522 | 52.93 | 52.96 | 53.00 | 84.39<br>84.36 | 15.39<br>15.43 | 84.52 | 15.48 | 20 |
| 2 | $C_{13}H_{28}$ | iso-$C_3H_7$ | $C_3H_7$ | 2,3,3,5,5-Pentamethyloctane | 68—68.5 (5) | 1.4428 | 0.7904 | 61.82 | 61.79 | 62.23 | 84.50<br>84.57 | 15.25<br>15.19 | 84.70 | 15.30 | 20 |
| 3 | $C_{13}H_{28}$ | iso-$C_3H_7$ | iso-$C_3H_7$ | 2,3,3,5,5,6-Hexamethylheptane | 75—75.4 (8) | 1.4455 | 0.7976 | 61.58 | 61.58 | 62.23 | 84.65<br>84.55 | 15.37<br>15.52 | 84.70 | 15.30 | 18 |
| 4 | $C_{15}H_{32}$ | iso-$C_4H_9$ | iso $C_4H_9$ | 2,4,4,6,6,8-Hexamethylnonane | 62—63 (2) | 1.4407 | 0.7852 | 71.38 | 71.36 | 71.47 | 85.02<br>84.97 | 15.03<br>14.98 | 84.80 | 15.20 | 15 |
| 5 | $C_{15}H_{32}$ | sec-·$C_4H_9$ | sec.-$C_4H_9$ | 3,4,4,6,6,7-Hexamethylnonane | 74.6—75 (2.5) | 1.4506 | 0.8102 | 70.50 | 70.56 | 71.47 | 84.65<br>84.67 | 15.31<br>15.26 | 84.80 | 15.20 | 6 |
| 6 | $C_{15}H_{32}$ | $C_2H_5-\underset{C_2H_5}{CH}-$ | iso-$C_3H_7$ | 2,3,3,5,5-Pentamethyl-6-ethyloctane | 112—113 (11) | 1.4520 | 0.8115 | 70.60 | 70.56 | 71.47 | 84.71<br>84.56 | 15.30<br>15.27 | 84.80 | 15.20 | 15 |
| 7 | $C_{17}H_{36}$ | iso-$C_5H_{11}$ | iso-$C_5H_{11}$ | 2,5,5,7,7,10-hexamethylundecane | 92—92.5 (2) | 1.4443 | 0.7926 | 80.62 | 80.64 | 80.71 | 84.92<br>85.01 | 15.16<br>15.05 | 84.90 | 15.10 | 10 |
| 8 | $C_{17}H_{36}$ | $C_3H_7-\underset{CH_3}{CH}-$ | $-\underset{CH_3}{CH}-C_3H_7$ | 4,5,5,7,7,8-Hexamethylundecane | 89—90 (1.5) | 1.4500 | 0.8098 | 79.82 | 79.85 | 80.71 | 84.96<br>85.05 | 15.10<br>15.09 | 84.90 | 15.10 | 3 |

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* $MR_D$ calculated by the additive scheme of V. M. Tatevskii with account of the subtypes of chemical bonds.

Addition of hydrogen chloride to the alkenes (II). The alkenes which we had synthesized were saturated with hydrogen chloride while cooled with ice and salt and then shaken for 2-3 days at room temperature with concentrated hydrochloric acid saturated while cold with hydrogen chloride. The resulting tertiary chlorides were washed with water, dried over calcium chloride, and vacuum-distilled (the yield of chlorides in all cases reached 90%). Some of the chlorides lost hydrogen chloride when distilled or kept: such unstable tertiary chlorides were reacted with organomagnesium compounds (in the presence of mercuric chloride) immediately after their preparation, washing with water, and drying (but without distillation); their constants were determined by distillation of a small amount of the substance (see Table 2).

Synthesis of di-tert-alkylmethanes (IV) from the tertiary chlorides (III). The reaction between the organomagnesium compounds (R'MgBr) and the tertiary chlorides was carried out in the presence of mercuric chloride by the method described in the previous communication [1]. The reaction products (after distilling off the ether) were shaken for an hour with concentrated hydrochloric acid at 40-60° (to decompose the mercury compounds of which were formed as contaminants in the reaction), washed with 2 N soda solution and water, dried over calcium chloride, and after boiling over sodium, they were distilled. In the following fractionations they were redistilled on a column with 30 theoretical plates and in each case two fractions were collected, the lower boiling of which corresponded to the starting alkene (II) in yield of about 50% and the higher boiling di-tert-alkylmethane. The constants, yields and analytical data for the di-tert-alkylmethanes (not previously described) are given in Table 3.

We should remark that for the branched alkanes (Nos. 2, 3, 5, 6, 8) in which there were adjacent quaternary and tertiary carbon atoms, the observed molecular refractions ($MR_D$) differed greatly (by 0.40-0.90) from the values calculated in the usual way (from the atomic refraction); therefore in Table 3 we give $MR_D$ also as calculated by the additive scheme of V. M. Tatevskii [10], calculated on subtypes of chemical bonds. The molecular refraction (calculated according to V. M. Tatevskii) agrees well with the results of our experiments.

Synthesis of di-tert-alkylmethanes was studied by the method of combination light scattering.* In none of the hydrocarbon spectra was there a frequency in the region 1600-1680 $cm^{-1}$, which shows the absence of any contaminating unsaturated hydrocarbons. The presence of complex branching with quaternary atoms of carbon was confirmed in all cases by the presence of intense spectral lines in the regions 690-740, 930, and 1200-1250 $cm^{-1}$ [11, 12].

Synthesis of 3,3,5,5-tetramethylheptane from 2,4-dichloro-2,4-dimethylpentane. The reaction between ethylmagnesium bromide (115 g of ethyl bromide, 24.3 g of magnesium, and 200 mg of absolute ether) and 2,4-dichloro-2,4-dimethylpentane [(V), 0.25 mole] was carried out in the presence of mercuric chloride under the conditions [1] described for the reaction between R'MgBr and saturated tertiary monochlorides (III). When the reaction product was distilled we obtained a 5% yield (based on the dichloride) of 3,3,5,5-tetramethylheptane with constants close to those obtained earlier by us [1] for this hydrocarbon (b.p. 71-73° at 12 mm, $n^{20}D$ 1.4327, $d^{20}_4$ 0.6793), and also the dimer of 2,4-di-methyl-1,3-pentadiene (b.p. 92° at 12 mm).

## SUMMARY

1. We have worked out a new general method based on 2,4-dimethyl-1,3-pentadiene for the synthesis of alkanes with two quaternary carbon atoms separated by a $CH_2$ group (di-tert-alkylmethanes); these have been difficult to obtain and were almost unknown earlier, since only the first member of this series of hydrocarbons had been described. The method consists of the following reactions: 1) obtaining a tertiary unsaturated chloride of the allyl type by treatment of 2,4-dimethyl-1,3-pentadiene with hydrogen chloride; 2) its reaction with alkyl magnesium bromides to give alkenes with one quaternary carbon atom (yields 45-65%); 3) treatment of these with hydrogen chloride; 4) reaction of the tertiary chlorides thus obtained (in yields of 90%) with alkylmagnesium bromides in the presence of mercuric chloride.

2. We have synthesized di-tert-alkylmethanes with symmetrical and unsymmetrical structures, including those in which there are neighboring quaternary and tertiary carbon atoms (yield 3-20% based on the tertiary chloride which reacts, and 6-40% based on that used in the reaction).

3. We have described for the first time some tertiary monochlorides with one quaternary carbon atom in the chain.

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* We express thanks to E. G. Treshchova for carrying out the optical studies.

4. We have worked out a method for preparing the hydrogen chloride addition products of 2,4-dimethyl-1,3-pentadiene with the separation of its monochloride (2-chloro-2,4-dimethyl-3-pentene) and its dichloride (2,4-dichloro-2,4-dimethylpentane).

## LITERATURE CITED

[1] R. Ia. Levina, Iu. S. Shabarov, V. K. Daukshas, and E. G. Treshchova, DAN SSSR 113, 102 (1957).*

[2] R. Ia. Levina, A. A. Fainzil'berg, and N. P. Shusherina, Zh. O. Kh. 18, 1775 (1948).*

[3] R. Ia. Levina, A. M. Paniushkina, N. A. Shcheglova, N. A. Smirnova, K. D. Shcherbakova, and I. A. Shor, Zh. O. Kh. 11, 411 (1941).

[4] R. Ia. Levina and Iu. B. Kagan, Zh. O. Kh. 11, 523 (1941).

[5] R. Ia. Levina and S. A. Egorova, Zh. O. Kh. 16, 821 (1946).

[6] R. Ia. Levina, Iu. S. Shabarov and V. K. Daukshas, Vestn. MGU, ser. matem., mekhan, astr., fiz., i khim., No. 1 (1958).

[7] D. V. Tishchenko, Zh. O. Kh. 9, 1386 (1939).

[8] A. Baeyer, and V. Villiger, Ber. 33, 858 (1900).

[9] F. C. Whitmore, H. A. Southgate, J. Am. Chem. Soc. 60, 2571 (1938).

[10] V. M. Tatevskii, The Chemical Structure of Hydrocarbons and Regularities in Their Physicochemical Properties, Izd. MGU, 287-296 (1953).**

[11] B. I. Stepanov, Zh. F. Kh. 20, 917 (1946).

[12] E. G. Treshchova, P. A. Akishin, and V. M. Tatevskii, Zh. A. Kh. 3, 75 (1948).

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# A STUDY OF THE CHEMICAL STRUCTURE OF SODIUM-CARBONIC ACID POLYMERS OF DIVINYL

A. I. Iakubchik, A. I. Spasskova, and L. A. Shibaev

Sodium-carbonic acid polymers of divinyl are formed when divinyl is polymerized by metallic sodium in an atmosphere of dry carbon dioxide [1, 2]. It is a friable, spongy product, not swollen and not soluble in the ordinary organic solvents. In contact with divinyl and its homologs, it can cause the formation of polymers like itself.

Steimmig found levulinic aldehyde and levulinic acid in the decomposition product of the ozonide of the sodium-carbonic acid polymer of isoprene. Hence, in the polymer, the isoprene molecules are combined in the 1,4-position (about 80% of the carbon skeleton of the polymer) [2].

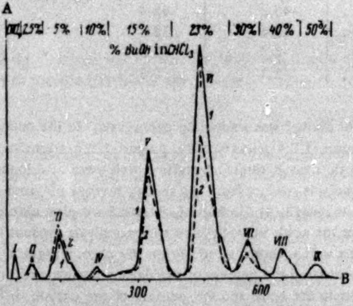

Fig. 1.

1) Chromatogram of the viscous acid from the product of ozonolysis of sodium-carbonic acid polymer (20°); 2) chromatogram of an acid mixture of levulinic (II), acetic (III), formic (IV), succinic (V), butan-1,2,4-tricarboxylic (VI) and propan-1,2,3-tricarboxylic (VII) acids; A) amount of alkali (in mg); B) amount of extracting solvent (in ml)

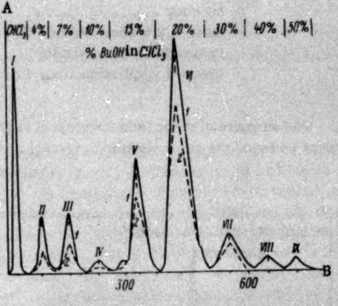

Fig. 2.

1) Chromatogram of the viscous acid from the ozonolysis product of sodium-carbonic acid polymer (50°); 2) chromatogram of an acid mixture: levulinic (II), acetic (III), formic (IV), succinic (V), butan-1,2,4-tricarboxylic, (VI), propan-1,2,3-tricarboxylic (VII); A) amount of alkali (im mg); B) amount of extracting solvent.

When we studied the chemical structure of the sodium-carbonic acid polymer of divinyl obtained at 20 and 50°, we showed that in this polymer a considerable percentage of the divinyl molecules are combined in the 1,4-position and their structure is very similar to the structure of the spongy polymer of divinyl [3]. In Table 1 we give data on the chemical structure of sodium-carbonic acid and of spongy polymer of divinyl. Although their structure is very similar to the structure of the rubber-like polymer, their properties are very different from sodium divinyl rubber. The absence of elasticity in these polymers and their insolubility evidently depend not only on chemical structure, but on other factors which determine the properties of high molecular-weight compounds.

TABLE 1

| | Percent of divinyl molecules combined in position | |
|---|---|---|
| | 1.4 | 1.2* |
| Spongy divinyl polymer | 55.5 | 22.8 |
| Sodium-carbonic acid divinyl polymer obtained at 50° | 54.4 | 23.6 |
| Sodium-carbonic acid divinyl polymer obtained at 20° | 57.1 | 20.1 |

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* The percent of 1,2-bonds was determined by the amount of HCOOH and HCOH in the ozonolysis product.

TABLE 2

| Acid | Percent of the hydrocarbon skeleton in the acids found in the ozonolysis products of the polymers prepared at | |
|---|---|---|
| | 20° | 50° |
| Leculinic | 0.8 | 2.2 |
| Succinic | 46.3 | 42.4 |
| Butan-1,2,4-tricarboxylic | 11.4 | 12.5 |
| Propan-1,2,3-tricarboxylic | 2.7 | 2.3 |
| Hexan-1,x,y,6-tetracarboxylic | 2.3 | 0.5 |

The structure of the sodium-carbonic acid polymer of divinyl was studied by ozonolysis. In the ozonolysis product we found the acids: levulinic, formic, succinic, butan-1,2,4-tricarboxylic, propan-1,2,3-tricarboxylic, and hexan-1,x,y,6-tetracarboxylic which were also found in the ozonolysis product from the spongy divinyl polymer and divinyl rubber [3, 4]. In Figs. 1, 2, and 3 we give chromatograms of the acids isolated from the ozonolysis product of the polymers which were studied. From the chromatograms we have calculated the percent of the carbon skeleton of the polymers in the acids and the percent of the carbon skeleton of the polymers in the portions from which they were formed in the ozonolysis. The results are given in Tables 2 and 3.

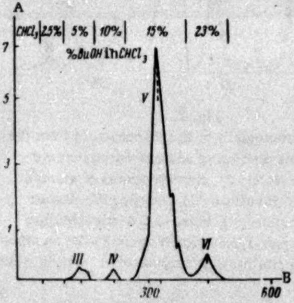

Fig. 3. Chromatogram of the separation of the crystalline acid from the ozonolysis product of sodium-carbonic acid polymer (20°).

In the portions with known structure are found 64-66% of the carbon skeleton of the polymers. In the products of oxidative decomposition of the ozonides of the polymers which were studied are found 89-90% of the carbon skeletons of the ozonized polymers. The carbon skeleton of the polymers which is not accounted for was contained in acids whose structure was not determined and which on chromatogram 1 (Figs. 1 and 2) correspond to peaks I and IX, and also in the neutral and gaseous products which we did not study. Also there are peaks on the chromatograms which corresponds to acetic and formic acids. Acetic acid could be formed in the isomerization of a portion with exterior double bonds [5] and in the decomposition of levulinic acid in an oxidizing medium. We could not calculate the acetic acid because the oxidative decomposi-

TABLE 3

| Name of acid | Structural portion of the polymer from which the acid was formed | Percent of the carbon skeleton of the polymer in the portion | | Percent of combined divinyl in positions 1,4 and 1,2 in polymers obtained at | | | |
|---|---|---|---|---|---|---|---|
| | | polymer obtained at | | 20° | | 50° | |
| | | 20° | 50° | 1,4 | 1,2 | 1.4 | 1,2 |
| Levulinic. . . . . . . . | -1,4-1,2-1,4- | 1.2 | 3.4 | 0.6 | 0.6 | 1.7 | 1.7 |
| Succinic . . . . . . . . | -1,4-1,4- | 46.3 | 42.4 | 46.3 | – | 42.4 | – |
| Butan-1,2,4-tri-carboxylic . . . . . | -1,4-1,2-1,4- | 13.0 | 14.2 | 6.5 | 6.5 | 7.1 | 7.1 |
| Propan-1,2,3-tricar-boxylic | -1,4-1,4-with branching at the α-methyl-ene group* | 2.7 | 3.0 | 2.7 | – | 3.0 | – |
| Hexan-1,x,y,6--tetracarboxylic | $-1,4-(-1,2-)_2-$ -1,4- | 2.8 | 0.6 | 1.0 | 1.8 | 0.2 | 0.4 |
| | | 66.0 | 63.6 | 57.1 | 8.9 | 54.4 | 9.2 |

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* Also, propan-1,2,3-tricarboxylic acid can be formed from the portion -1,4-1,2-1.4- as an abnormal ozonolysis product [5].

tion of the ozonide was carried out in glacial acetic acid. Formic acid, formed in abnormal ozonolysis, was removed in the distillation of the solvent.

## EXPERIMENTAL

The polymerization of divinyl by metallic sodium was carried out in an atmosphere of dry carbon dioxide at 20 and 50°. Divinyl was obtained by reduction of tetrabromobutane (b.p. 118°) with zinc in an aqueous alcohol medium, dried over calcium chloride, and distilled over sodium. The ampules in which the polymerizations were carried out were carefully dried. The air was driven out of them by heating and they were filled with dry carbon dioxide. This was repeated several times. The ampules were cooled to −50° and filled with divinyl into which sodium was introduced in the form of a wire (1% of the weight of divinyl). All operations were carried out in an atmosphere of carbon dioxide which was carefully freed from moisture, HCl, and traces of oxygen [6]. The polymerization was carried out in an air thermostat. The temperature of the thermostat was held to ± 0.2°. Polymerization at 20° lasted five months. The length of the polymerization at 50° was 300 hours. The polymerization was characterized by a large induction period, at the end of which the sodium wire became gray and increased in volume. The transformation of the divinyl into the sodium-carbonic acid polymer occurred with a great increase in volume. Polymerization at 50° was accompanied by a greater increase in volume than polymerization at 20°. In the process of this increase the polymer exerted great pressure on the walls of the ampules. To remove traces of sodium, the polymer was treated with alcohol. After purification the sodium-carbonic acid polymer of divinyl, it was a spongy, nonelastic, very light product which kept the form of the sodium wire.

In the polymer obtained at 20° we found %: C 86.97, 87.17; H 11.01, 11.11.

In the polymer obtained at 50° we found %: C 86.16, 86.10; H 11.28, 11.15. $(C_4H_6)_x$. Calculated %: C 88.89; H 11.11.

Ozonization of the sodium-carbonic acid polymer of divinyl was carried out in ethyl acetate, using oxygen which contained 5% ozone at a rate of passage of the gas through the apparatus of 13 liters per hour. The sodium-carbonic acid polymer ozonized slowly. A sample of 1.5-2 g was ozonized in 20 hours. We ozonized 6.75 g of the 20° polymer which contained 5.88 g of carbon, and 5.18 g of the 50° polymer which contained 4.46 g of carbon. The resulting ozonides were soluble in ethyl acetate. The solvent was distilled off by passing dry air at 15-10 mm

TABLE 4

| Separated acid mixture | Peak of volume | | | | | |
|---|---|---|---|---|---|---|
| | II | III | IV | V | VI | VII |
| | levulinic acid | acetic acid | formic acid | succinic acid | butanetri-carboxylic acid | propane tricarboxylic acid |
| Viscous acid from the ozonolysis product of the 20° polymer . . . . . | 54 | 117 | 246 | 342 | 464 | 546 |
| Mixture of expected acids. . . . . . . . | 54 | 117 | 241 | 342 | 464 | 544 |
| Viscous acid from ozonolysis product of the 50° polymer. . . . . . . . . . . | 60 | 120 | 210 | 336 | 468 | 551 |
| Mixture of expected acids. . . . . . . . | 60 | 120 | 213 | 336 | 468 | 553 |

TABLE 5

| Acids | Weight of acid (in mg) in the ozonolysis product of polymers obtained at | |
|---|---|---|
| | 20° | 50° |
| Levulinic. . . . . . . . . . . . . . . . . . . . | 94 | 189 |
| Acetic . . . . . . . . . . . . . . . . . . . . . | 233 | 554 |
| Succinic . . . . . . . . . . . . . . . . . . . . | 768 | 320 |
| Butan-1,2,4-tricarboxylic . . . . . . . . . . | 1526 | 1257 |
| Propan-1,2,3-tricarboxylic . . . . . . . . . | 395 | 233 |
| Hexan-1,x,y,6-tetracarboxylic. . . . . . . | 294 | 50 |

and 20°. The ozonide was a colorless, viscous substance. Oxidative decomposition of the ozonide was carried out with acetyl hydroperoxide in a solution of glacial acetic acid cooled to 0°. Acetyl hydroperoxide was added to the ozonide in the following amounts: at first one atom of active oxygen per double bond in the sample of polymer used for the ozonolysis, and after a day,twice the volume of hydroperoxide was added and the mixture stood for several days until complete decomposition of the ozonide had occurred. The excess acetylhydroperoxide was decomposed by platinum black at 25°. Acetic acid was distilled from the product of oxidative decomposition of the ozonide at 10-4 mm and 30° to constant weight of acid. The viscous acid was separated from the crystals by solution of the first in diethyl ether. After removal of the ether we obtained 6.31 g of viscous and 6.34 g of crystalline acid from the 20° polymer and 5.13 g of viscous and 4.23 g of crystalline acid from the 50° polymer. In these acids we found 5.3 g of carbon or 90% of the carbon skeleton of the 20° polymer, and 3.9 g of carbon or 89% of the carbon skeleton of the 50° polymer. The melting point of the crystalline acid was 179-180°. After it was recrystallized from hot water it melted at 184-185°. Mixed melting point with succinic acid (m.p. 184°) was 184-185°. Separation of the acids was carried out chromatographically on MSK silica gel, as described earlier [3, 7]. In Figs. 1 and 2 we give the chromatograms of the separation of the viscous acid from the ozonolysis product of the polymers which we studied, and the mixture of acids: levulinic, acetic, formic, succinic, butan-1,2,4-tricarboxylic, and propan-1,2,3-tricarboxylic which were earlier found in the ozonolysis products of the spongy divinyl polymer. The acids were identified by their volume peaks [8, 9]. In Table 4 we give the volume of the peaks of the studied and expected acids.

The separations of the viscous acids isolated from the ozonolysis of the polymers studied were carried out on different columns, and so the peaks do not entirely agree.

From Figs. 1 and 2 and Table 4 it follows that in the chromatograms of the mixtures which were studied, peak II corresponds to levulinic acid, III to acetic, IV to formic, V to succinic, VI to butan-1,2,4-tricarboxylic, VII to propan-1,2,3-tricarboxylic, and VIII to hexan-1,x,y,6-tetracarboxylic acid.* In peaks I and IX the nature of the acid was not established. We ran the separation of the crystalline acid under the same conditions. In Fig. 3 we give the chromatogram for the separation of the crystalline acid from the product of ozonolysis of the polymer obtained at 20°. The chromatogram for the separation of the crystalline acid from the ozonolysis products of the 50° polymer was analogous to that given in Fig. 3. The crystalline acid is 95% succinic acid (peak V). There are no other acids in the acetic acid distilled from the decomposition products of the ozonide. From the chromatograms of the viscous and crystalline acids we can calculate the amounts of each acid in the ozonolysis products from the polymers studied. The results are given in Table 5.

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*It was shown that the acid washed from the column by 40% butanol was hexan-1,x,y,6-tetracarboxylic acid [7].

Succinic acid isolated from the crystalline acid made up 41% of the carbon skeleton of the 20° polymer and 39.5% of the carbon skeleton of the 50° polymer.

The percent of outer double bonds was calculated on the basis of the amount of formic acid and formaldehyde in the ozonolysis products of the polymers studied [10]. In sodium-carbonic acid polymers obtained at 20° there were 20.1%, in the 50° polymers, 23.6% of links with outer double bonds.

## SUMMARY

1. We have shown that the structure of the sodium-carbonic acid polymer of divinyl is very close to the structure of the spongy polymer of divinyl.

2. The chemical structures of the sodium-carbonic acid polymers obtained at 20 and 50° are practically the same.

## LITERATURE CITED

[1] K. Harries, Untersuchungen über die natürlichen and künstlichen Kautschukarten (1919).

[2] G. Steimmig, Ber. 47, 350 (1914).

[3] A. I. Iakubchik and A. I. Spasskova, Zh. O. Kh. 28, 143 (1958).*

[4] A. I. Iakubchik and Academician S. V. Lebedev, Izd. AN SSSR 206 (1954).

[5] C. S. Marvel et al, J. Org. Ch. 16, 838 (1951).

[6] Iu. V. Karlankin, Pure Chemical Reagents, p. 74 (1954).**

[7] A. I. Iakubchik and S. K. Zykova, Zh. P. Kh. 29, 1591 (1956).*

[8] A. N. Fuks and L. S. Chetverikova, Zh. A. Kh. 3, 220 (1943).

[9] N. A. Fuks, Reactions and Methods of Investigation of Organic Compounds, I, 181 (1951).**

[10] A. I. Iakubchik, A. A. Vasil'ev, and V. M. Zhabina, Zh. P. Kh. 17, 107 (1944).

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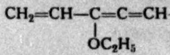
# THE SYNTHESIS OF ALKOXY DERIVATIVES OF DIVINYLACETYLENE

## VII. THE DIRECTION OF ADDITION OF ETHYL ALCOHOL TO DIVINYLACETYLENE

A. L. Klebanskii and D. M. Krasinskaia

In a previous communication [1] it was shown that different alcohols added in different directions to divinylacetylene under the influence of sodium alcoholate or alcoholic solutions of sodium hydroxide at the boiling point of the mixtures. Thus, methyl alcohol added in the 1,4-position (at 60-65°), ethyl in position 1,6 (at 85-95°). We might expect that the different directions of addition would depend on the reaction temperature or the structure of the radicals. In order to explain the effect of reaction temperature on the direction of addition of ethyl alcohol to divinylacetylene, in the present work we have studied its reaction under the influence of sodium alcoholate at a lower temperature (60°) corresponding to the reaction temperature of methyl alcohol. We then found the addition of ethyl alcohol to divinylacetylene occurred preferably in the 1,4-position, as for methyl alcohol. The rate of addition of ethyl alcohol was much less than for methyl alcohol at the same temperature. The yield of ethoxy derivative in 300 hours was 14% of the starting hydrocarbon, and of the methoxy derivative, 12-13% of the starting hydrocarbon in 40-60 hours.

The product of addition of ethyl alcohol was 3-ethoxy-1,3,4-hexatriene (I). The structure of this compound was shown by ozonization which gave formic, acetic, and oxalic acids. Thus, it was shown that the direction of addition of ethyl alcohol to divinylacetylene depended on the reaction temperature.



$CH_2{=}CH{-}\underset{OC_2H_5}{\underset{|}{C}}{=}C{=}CH{-}CH_3$ ( )

$C_2H_5O{-}CH_2{-}CH{=}C{=}C{=}CH{-}CH_3$ (II)

In order to establish whether 1-ethoxy-2,3,4-hexatriene (II), which corresponds to 1,6-addition, obtained at 85-95°, was an isomerization product of I (1,4-addition) which was obtained at lower temperature (60°), we heated the latter at 100° for 29 hours in the presence of sodium alcoholate. The main mass of the product which was isolated had the constant of the products of 1,6-addition, that is, 1-ethoxy-2,3,4-hexatriene. In ozonolysis it formed a mixture from which we isolated the silver salts of acetic and ethoxyacetic acids and traces of formic acid; oxalic acid was absent. These results allow us to assume that the primary direction of the reaction is the addition in the 1,4-position; the product of this addition undergoes an allyl rearrangement under the influence of alcoholic alkali at higher temperatures to a compound which corresponds to 1,6-addition.

In order to see whether there is also addition of methyl alcohol to divinylacetylene in the 1,6-position at higher temperatures, we studied this reaction at 100°. However, the increased temperature caused polymerization of the reaction products. Individual compounds were not isolated. This indicates the greater rate of polymerization of methoxy derivatives of divinylacetylene compared to the corresponding ethoxy derivatives.

The results allow us to assume that the primary direction of addition of ethyl alcohol under the influence of sodium alcoholate or alkali is in the 1,4-position. At higher temperatures there occurs an isomeric rearrangement into the 1,6-position. For the methoxy group, because of the great rate of polymerization at higher temperatures, we cannot isolate the products of the isomeric rearrangement.

It is possible that the results on the different directions of addition of methyl alcohol to vinylacetylene obtained by Carothers and co-workers [2] by heating with alcoholic alkali to 105°, and by I. A. Rotenberg and M. A. Favorskaia [3] at 150°, are also due to the temperature of the reaction.

## EXPERIMENTAL

Reaction of divinylacetylene with ethyl alcohol at 60°. A mixture of 78 g (1 g mole) of divinylacetylene (b.p. 29-30° at 100 mm, $d^{20}_4$ 0.7850, $n^{20}D$ 1.503) with a solution of 6.55 g of sodium in 187 g of anhydrous alcohol was heated in a flask with a reflux condenser for 300 hours at 60° in a nitrogen atmosphere. After the heating, the alcoholate was decomposed by saturating with dry carbon dioxide. After the sodium carbonate had been removed, the filtrate was distilled. We obtained two fractions. The distillate from the first fraction consisted of an alcoholic solution of divinylacetylene; the latter was separated by salting out with a sodium chloride solution with later drying and redistilling. We obtained 33.5 g of divinylacetylene; that is, 43% of that taken at the beginning (b.p. 30-30.5° at 100 mm, $n^{20}D$ 1.502). The products of the 2nd fraction in the amount of 10.9 g (14% of the weight of hydrocarbon used) had b.p. 40-60° at 1-2 mm. The tarry residue in the distilling flask weighed 19.1 g (24.5%) of the weight of starting hydrocarbon. The loss, mostly of divinylacetylene, was 14.4 g (18.5% of the weight of starting hydrocarbon). By repeated distillation of the 2nd fraction we obtained a substance:

B.p. 48-50° at 1-2 mm, $d^{20}_{20}$ 0.8591, $n^{20}D$ 1.4665, $MR_D$ 39.94; calc. 39.386.

Found %: $C_2H_5O$ 36.86, M 122. $C_8H_{12}OF_3$. Calculated %: $C_2H_5O$ 36.3, M 124.

Ozonization of 3-ethoxy-1,3,4-hexatriene (I). 5.4 g of the above described substance was dissolved in 180 ml of dry, purified chloroform. At −40° oxygen which contained ozone was passed through the solution. The ozone concentration was 5.4%. At the end of the ozonization the chloroform was distilled off at 30-33° (1-2 mm). The residue was a glycerol-like, light-yellow oil. It was treated with 40 ml of a 4% solution of hydrogen peroxide for 15 hours at 0-20°, and then for 4 hours at 100°. Treatment with hydrogen peroxide was continued until the reaction for aldehyde groups stopped. The excess hydrogen peroxide was decomposed at 100° in the presence of palladium black. After the catalyst had been separated, the filtrate was distilled. This gave a water solution of volatile acids and 3.3 g of thick, sirupy liquid in the residue. In an aliquot portion of the volatile-acid solution formic acid was determined by calomel. The total amount of calomel, on conversion to the sum of volatile acids, was 3.346 g, which corresponds to 0.326 g of formic acid or 16% of the calculated amount. The low yield of formic acid was evidently caused by its decomposition when the solution was heated with hydrogen peroxide and palladium black. When the residue of aqueous solution of volatile acids was heated with freshly precipitated silver oxide, 5.56 g of silver salts formed. Evaporation of the mother liquor from the silver salts gave 0.5 g more salt, so that the total was 6.06 g (83%). The silver salts were studied gravimetrically.

Found %: Ag 64.20 (from the main mass of salts) and 63.54 (from the mother liquors). $C_2H_3O_2Ag$. Calculated %: Ag 64.26.

The thick, sirupy liquid (3.3 g) remained after distillation of the acetic and formic acids and gave a positive reaction for oxalic acid. The water solution of this acid was treated with activated charcoal and concentrated. Crystals with m.p. 100.5° separated. A mixed melting point with oxalic acid dihydrate melted at 101°. The yield of oxalic acid calculated on the residue was 84%.

Isomerization of 3-ethoxy-1,3,4-hexatriene. 6 g of the substance (b.p. 48-50° at 1-2 mm, $d^{20}_{20}$ 0.8592, $n^{20}D$ 1.4665) was heated 29 hours at 100° with a solution of 1 g of metallic sodium in 35 g of anhydrous alcohol. After heating, the reaction mass was treated in the same way as in the previous experiment. Distillation gave two fractions: the 1st, 44-45° at 4-5 mm, $d^{20}_{20}$ 0.8626, $n^{20}D$ 1.4675, 1.6 g; the 2nd, 83-84° at 1-2 mm, $d^{20}_{20}$ 0.8607, $n^{20}D$ 1.4670, 1.4 g. The tarry, nonvolatile residue in the distilling flask was 1.5 g.

Because of the small quantity of product in each fraction, their separation was not sufficiently sharp. The constants of the products of the 1st fraction correspond more to those of 1-ethoxy-2,3,4-hexatriene (b.p. 43-44° at 4 mm, $n^{20}D$ 1.4685, $d^{20}_{20}$ 0.8628) than to those of the starting 1-ethoxy-1,3,4-hexatriene. To establish the structure of the product which we obtained, we submitted 1.35 g of the 1st fraction to ozonolysis. The conditions of the reaction and study of the products of decomposition of the ozonide were the same as described above. The water solution of the acids gave a positive reaction for formic and a negative reaction for oxalic acid. The amount of formic acid determined showed that it was present only as a slight admixture. Silver salts were obtained from the acid solution as described above. They could not be separated by crystallization.

Found %: Ag 58.6. $C_2H_3O_2Ag$. Calculated %: Ag 64.26. $C_4H_7O_3Ag$. Calculated %: Ag 50.91.

The value found for silver in the salts (58.6%) corresponds to 42.5% ethoxyacetic and 57.5% acetic acid. The data of the ozonolysis give reason to suppose that the studied isomerization product has the structure of 1-ethoxy-2,3,4-hexatriene.

## SUMMARY

1. We have established that at lower reaction temperatures of divinylacetylene and ethyl alcohol (60°) there occurs preferably addition of alcohol in the 1,4-position instead of the 1,6-position which we found at 85-95°.

2. We have shown that the product of addition of ethyl alcohol to divinylacetylene in the 1,4-position isomerizes on long heating in the presence of sodium alcoholate to give a compound with physical properties close to those of the product of addition in the 1,6-position. This gives a basis for supposing that the primary position of addition is the 1,4-position and that this, as the result of an isomeric rearrangement, is transformed into the 1,6-addition compound.

## LITERATURE CITED

[1] A. L. Klebanskii, D. M. Krasinskaia, and L. G. Safonova, Zh. O. Kh. 16, 1213 (1946).

[2] R. A. Jocobson, B. H. Dykstra and W. H. Carothers, J. Am. Chem. Soc. 56, 1169 (1934); Zbl. 1935, 1, 1210.

[3] I. A. Rotenberg and M. A. Favorskaia, Izv. AN SSSR, OKhN 1935, 219; Zh. O. Kh. 6, 185 (1936).

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# STUDIES IN THE FIELD OF POLYMETHYLENE RINGS

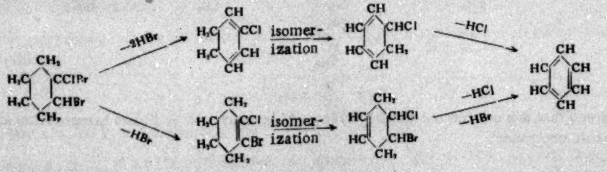
## XXXI. THE REACTION OF 1-CHLORO-1,2-DIBROMOCYCLOHEXANE WITH QUINOLINE

N. A. Domnin and V. A. Cherkasova

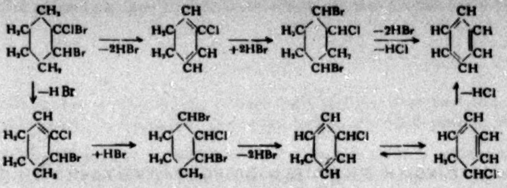
We showed earlier that in the reaction of 1-chloro-1,2-dibromocylohexane with quinoline, chlorobenzene was formed [1]. We then showed the presence of chlorobenzene by the nitration method. However, even at that time there were indications in the literature that sometimes nitrosubstituents of benzene and its homologs could be formed partly by nitration of unsaturated cyclohexane hydrocarbons [2]. Later we showed that in the action of a nitrating mixture on methylcyclohexene and methyl-1,3-cyclohexadiene which did not contain toluene, 2,4-dinitrotoluene was formed [3]. After these findings, we were forced to give up the classical method of nitration as a method for showing the structure of the aromatic hydrocarbons and their halogen derivatives which were formed in these cases, if any unsaturated cyclohexenes or cyclohexadienes or their halogen derivatives could be present as contaminants.

To study the structure of the products formed as a result of the reactions connected with halogenation and dehalogenation of unsaturated cyclohexane hydrocarbons and polyhalogen derivatives of cyclohexane, we used the method of absorption spectroscopy in the ultraviolet part of the spectrum since it was fully reliable [4]. When we studied the reaction of 1-chloro-1,2-dibromocylohexane with quinoline and investigated the products of this reaction by the above mentioned method, we showed, as we had earlier, that the chief reaction product was monochlorobenzene (46%). However, we also showed that along with chlorobenzene there was formed a considerable a amount of benzene and a little 1,3-cyclohexadiene. This fact was somewhat unexpected, but at the same time, very interesting; it did not fit the theory or the experimentally based mechanism of our scheme of reaction of linked halogenation and dehalogenation [5] and it forced us to further assumptions which widened and modernized this scheme.

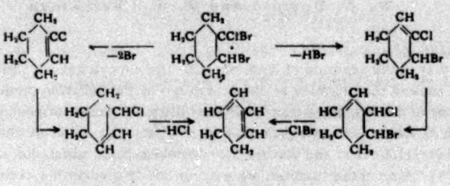
We can give some consideration to the mechanism of formation of benzene. In the reaction which we are discussing, quinoline hydrobromide is certainly formed, which, as was shown for the hydriodide [6] permits a shift of double bonds. In connection with this fact we have assumed a scheme of formation of monobromobenzene by the action of molecular bromine on 1,2-dibromo-1-cyclohexene and in the reaction of 1,1,2,2-tetrabromocyclohexane with quinoline [7]. A similar scheme can explain the formation of benzene in the reaction of 1-chloro-1,2-dibromocyclohexane with quinoline.



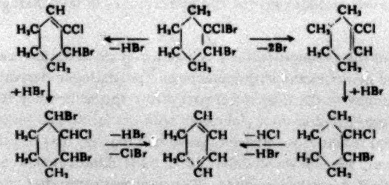
Along with this, however, for the formation of benzene in this reaction another scheme can be given, if we assume the possibility of splitting and combination of hydrogen bromide.



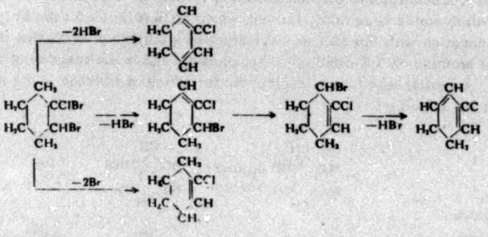
When we apply this idea of the mechanism of benzene formation to the case of simultaneous formation of 1,3-cyclohexadiene, we can offer the following scheme:



or



It was shown that along with chlorobenzene, benzene, and 1,3-cyclohexadiene, there was also formed 1-chloro-1-cyclohexene and 2-chloro-1,3-cyclohexadiene. Their formation fits completely into our scheme for the reaction mechanism of linked halogenation and dehalogenation and can be presented as follows:

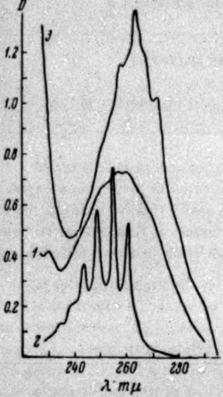


We showed that this unsaturated monochloride could be converted by linked halogenation and dehalogenation into an aromatic compound.

## EXPERIMENTAL

In a flask with a dropping funnel and a reflux condenser fitted with a calcium chloride tube was placed 15 g of 1-chloro-1,2-dibromocyclohexane and 10 g of quinoline. The contents were heated on an oil bath. At 130-135°

a very violent reaction began, during which heating was stopped and the flask was removed from the bath. At the end of the violent reaction, 30 g of chlorodibromide and 20 g of quinoline were gradually added through the dropping funnel at such a rate that it was not necessary to apply heat. At the end of the addition, when the reaction had evidently stopped, the contents were heated on the oil bath at 140-155° for 45 minutes, after which the reaction mixture was cooled by standing. The contents of the flask after standing overnight had formed two layers. The lower layer was a crystallized mass and the upper was an almost colorless liquid. The upper layer was poured into a Wurtz flask and 2 fractions were distilled from it: 85-135° (7 g) and 135-147° (5.7 g). The residue in the flask, a solid brown tar, was not studied. The attempt to isolate from the 85-135° fraction a more sharply boiling portion with a lower boiling point did not succeed. From both fractions we isolated a fraction with b.p. 132-140°



Absorption curves in the ultraviolet for the products of reaction of 1-chloro-1,2-dibromocyclohexane with quinoline.

The crystallized lower layer was heated to distill volatile products. We collected two fractions (distillation was accompanied by strong evolution of hydrogen halides) boiling at 83-100° (2.5 g) and 130-140° (5.45 g). The last fraction was combined with the 132-140° fraction obtained in the distillation of the upper, poured-off layer. Total weight 9.45 g. Redistillation of this fraction gave: 1) 0.28 g of a clear, mobile liquid with b.p. 85-95°, $n^{22.7}D$ 1.4647, which was energetically oxidized by potassium permanganate and whose absorption band in 0.01% alcohol solution in the ultraviolet in characteristics and position in the spectrum resembled the absorption bands of 1,3-cyclopentadiene (see Fig., Curve 1); 2) 8.4 g (46%) of a colorless liquid which boiled at 132-136°, $d_4^{17.7}$ 1.1058, $n^{17.7}D$ 1.5100, bromine number according to MacIllaney 9.07 [8], M 116.4, calculated for chlorobenzene 112.50. For a 0.01% alcohol solution of this fraction we took an absorption spectrum in the ultraviolet on an SF-11 (Fig., Curve 3). 7.4 g of the fraction was oxidized by potassium permanganate. However, the amount of potassium permanganate calculated for 2-chloro-1,3-cyclohexadiene was not used up. After treatment of the oxidation product we obtained 0.9 g of crystalline material which boiled at 149-150.5° and gave no depression with known adipic acid, and 0.14 g of crystals with m.p. 187-189° (the mixture in this case melted at 187.5-190°).

After a series of distillations from the fraction 83-100° we collected a portion boiling at 78.5-83° (1.8 g). At −2° it crystallized, $n^{16.1}D$ 1.5018, $d^{16.1}_4$ 0.8870. The bromine number according to MacIllaney was 3.7. The content of benzene, calculated by the bromine number, was 98.15% (see Fig., Curve 2, for 0.05% alcoholic solution).

## SUMMARY

1. By the method of absorption spectroscopy in the ultraviolet we have shown that in the reaction of 1-chloro-1,2-dibromocyclohexane with quinoline, besides 1-chloro-1-cyclohexene and 1-chloro-1,3-cyclohexadiene there is formed chlorobenzene (46%), if we consider that the fraction with b.p. 132-136° is chlorobenzene, benzene and small amounts of 1,3-cyclohexadiene.

3. We have suggested a scheme for the formation of benzene and 1,3-cyclohexadiene from 1-chloro-1,2-dibromocyclohexane.

## LITERATURE CITED

[1] N. A. Domnin and V. A. Cherkasova, Zh. O. Kh. 17, 2283 (1947).

[2] F. F. Vreden, Zh. R. F. Kh. O. 4, 256 (1872); O. Wallach, Ber. 24, 1573 (1891); Lieb. Ann. 258, 323 (1890); W. Markownikov, Lieb. Ann. 302, 7 (1898); C. Harries, and B. Antoni, Lieb. Ann. 328, 101 (1903); Pictet, Anal. Ch. [9] 10, 239 (1918); C. r. 163, 358 (1916); H. Maeyer, Lieb. Ann. 433, 350 (1923); S. S. Nametkin, Zh. O. Kh. 6, 1166 (1936).

[3] N. A. Domnin and V. A. Cherkasova, Zh. O. Kh. 26, 1166 (1956).*

[4] N. A. Domnin, V. A. Cherkasova, and S. N. Audreev, Zh. O. Kh. 21, 1818 (1951).*

[5] N. A. Domnin, Zh. O. Kh. 16, 29 (1946).

[6] A. E. Favorskii and I. I. Borgamn, Zh. R. Kh. O. 39, 1218 (1907).

[7] N. A. Domnin, Zh. O. Kh. 16, 1336 (1946).

[8] Standard Methods for Testing Petroleum and its Products, Ed. 5 (1944).

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*Original Russian pagination. See C.B. translation.

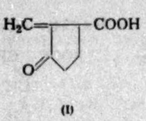
# STUDIES IN THE FIELD OF SARCOMYCIN AND ITS ANALOGS

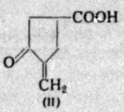
## II. SYNTHESIS OF SARCOMYCIN ISOMERS

M. M. Shemiakin, M. N. Kolosov, M. G. Karapetian, and V. Ia. Rodionov

In our first communication on the study of the chemistry of the anticancer antibiotic sarcomycin and its analogs we described the preparation of the optically active dihydrosarcomycin and its stereoisomer [1]. Continuing our studies in this field we present a study of methods of synthesis of sarcomycin itself (I). In carrying out this work, we synthesized an isomer of sarcomycin (II)(in the form of an ethyl ester), which differed from sarcomycin by a different position of the methylene group. This portion of our study is the subject of the present paper.

In spite of the simplicity of the structure of sarcomycin (I), the synthesis of the antibiotic is connected with specific difficulties because of the ease of oxidation of the compound and its great tendency to polymerization and isomerization [2]. Therefore, many methods which require the use of high temperatures for the reaction, or energetic reagents (especially alkaline or acid media) cannot be used for producing sarcomycin, whose characteristic group is β-methylene-γ-ketocarboxyl, and its formation is possible only with mild reagents in a limited range of pH values and at moderate temperatures.


(I)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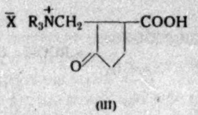
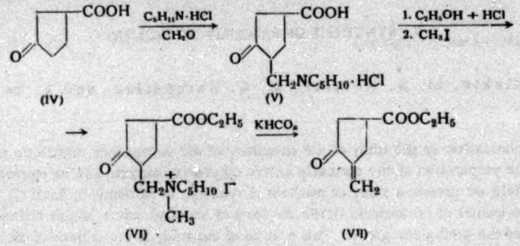

(III)

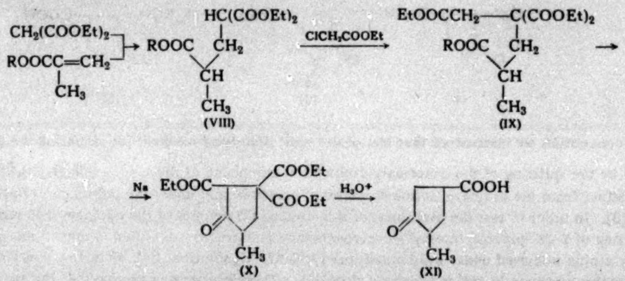
In this connection we considered that one of the most promising methods for preparing the desired unsaturated system would be the splitting of the quaternary ammonium compound of the type $-COCH(CH_2\overset{+}{N}R_3)-$, since this process (as distinct from the ordinary Hofmann splitting) proceeds only under the influence of $NaHCO_3$ at room temperature [3]. In order to test the usefulness of this method for ketones of the cyclopentane series we carried out a model splitting of 2-(N-piperidylmethyl)-cyclopentanone methiodide. We showed that in this case the splitting of the tertiary amine occurred under mild conditions (10% $KHCO_3$ solution, 20°, 48 hours), and led to formation of 2-methylenecyclopentanone in yields which reached 40%. Therefore we can assume that the analogous splitting of carboxy compounds of type III will go under these mild conditions and thus give a synthesis of sarcomycin itself (I).

The compounds of type III needed for the preparation of sarcomycin can be synthesized in different ways. One of the simplest of those which we considered is the synthesis of these compounds from the easily obtained cyclopentanone-3-carboxylic acid (IV) by direct introduction into position 2 of a dialkylaminomethyl group by the Mannich reaction with later treatment by alkyl halides to form the tertiary amine. It is true that such a scheme of synthesis offers equal possibility of introduction of the dialkylaminomethyl residue into positions 2 and 4 of the acid IV, and in the second case this would lead to the formation of a structural isomer of sarcomycin (II). Since in the condensation of the ketoacid IV with formaldehyde and piperidine hydrochloride we isolated only 4-(N-piperidylmethyl)-3-carboxylic acid (V), this method was shown to be suitable for the synthesis of isosarcomycin (II) and not for the antibiotic itself (I).

In carrying out the synthesis of isosarcomycin it was necessary to consider that this acid, like sarcomycin, probably would be an oil which could not be distilled and would not tend to form crystalline derivatives. At the same time, it is known [4] that the ester of one acid of this type, namely 2-ethylidene-cyclopentanone-3-carboxylic acid, can be purified by distillation. Therefore the aminoketoacid which we obtained (V) was first esterified and only then was the methiodide prepared. The ethyl 4-(N-piperidylmethyl)-cyclopentanone-3-carboxylate methiodide (VI) [analogous to the 2-(N-piperidylmethyl)-cyclopentanone methiodide which we studied earlier] could be easily split at room temperature in the presence of 10% $KHCO_3$ solution to give 45% yield of the ethyl ester of isosarcomycin (VII) which could be purified by vacuum distillation.


COOH
$C_5H_{11}N \cdot HCl$
$CH_2O$
O
(IV)
COOH
O
$CH_2NC_5H_{10} \cdot HCl$
(V)
1. $C_2H_5OH + HCl$
2. $CH_3I$
$COOC_2H_5$
O
$CH_2\overset{+}{N}C_5H_{10}\ I^-$
$CH_3$
(VI)
$KHCO_3$
$COOC_2H_5$
O
$CH_2$
(VII)

The structure of this ester of isosarcomycin was established as follows: 1) the presence in its molecule of a double bond was shown by ozonolysis with formation of formaldehyde; 2) the relation of the carbonyl and methylene groups to the carboxyl was shown by catalytic hydrogenation of the compound to the corresponding saturated ketoester and its hydrolysis to a crystalline methylcyclopentanone carboxylic acid; the latter was different from racemic dihydrosarcomycin, but identical with 4-methylcyclopentanone-3-carboxylic acid especially synthesized by the following scheme:*


$CH_2(COOEt)_2$
$ROOCC{=}CH_2$
$CH_3$
$HC(COOEt)_2$
ROOC
$CH_2$
CH
$CH_3$
(VIII)
$ClCH_2COOEt$
$EtOOCCH_2$
$C(COOEt)_2$
ROOC
$CH_2$
CH
$CH_3$
(IX)
Na
EtOOC
COOEt
COOEt
O
$CH_3$
(X)
$H_3O^+$
COOH
O
$CH_3$
(XI)

Since we showed that in direct condensation of the ketoacid IV with formaldehyde and piperidine hydrochloride the dialkylamino group enters position 4, we decided to protect this more reactive position in the molecule by the easily removed N-methylanilinomethylene group so that the condensation could be directed into the desired 2-position. The possibility of running the Mannich reaction with compounds of this type was studied by us on 2-(N-methylanilinomethylene)-cyclopentanone (XII). This showed that introduction of the N-methylanilinomethylene group in the α-position to the keto group so strongly deactivated the carbonyl group that under the ordinary conditions of the Mannich reaction, the starting compound only underwent hydrolysis and then formed a tar, and under anhydrous conditions did not change, but also did not undergo condensation.

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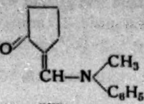
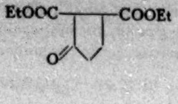
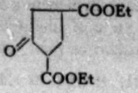
* The 4-methylcyclopentanone-3-carboxylic acid described in the literature, in distinction to the compound which we obtained, is a non-crystallizing oil [5].


(XII)


(XIII)


(XIV)

We made one other attempt to synthesize a compound of type III by directed introduction of the dialkylaminomethyl group into the desired position in the cyclopentanone ring. As is known, α-substituted β-ketoacids usually easily undergo the Mannich reaction with simultaneous decarboxylation [6]. Hence we hoped that if we started from 3-cyclopentanone-1,2-dicarboxylic acid, we could introduce the dialkylaminomethyl group in position 2. Therefore the diethyl ester of this acid (XIII) [1] was saponified with 1 N KOH at room temperature and then, under ordinary conditions, submitted to condensation with piperidine hydrochloride and formaldehyde. However, at 0-30° the reaction proceeded especially slowly (at higher temperatures there was rapid decarboxylation of the β-ketoacid) and no crystalline products could be isolated.* We should mention that the analogous condensation of the previously saponified ketodiester (XIV) also goes very sluggishly, but in this case it is possible to isolate the aminoketoacid hydrochloride, though in yields of less than 1%.

## EXPERIMENTAL

1. 2-(N-piperidylmethyl)-cyclopentanone methiodide. To a solution of 48.6 g (0.22 mole) of 2-(N-piperidylmethyl)-cyclopentanone hydrochloride [7] in 100 ml of water was added 160 ml of 40% $K_2CO_3$ solution; the base which formed was extracted with ether, the extract dried with $CH_3COOK$ and evaporated in a vacuum. The resulting 2-(N-piperidylmethyl)-cyclopentanone, without preliminary distillation (the pure substance had b.p. 81° at 1 mm, $n^{20}D$ 1.4887), was dissolved in 75 ml of dry acetone and 43.2 g (0.24 mole) of methyl iodide was added with stirring; the mixture was stirred for 1.5 hours more and allowed to stand at 20-25° for 36 hours. The precipitate was filtered and washed with acetone and ether. Yield 66.4 g (92%), m.p. 124-125° (from alcohol).

Found %: C 44.40; H 6.81; N 4.11; I 39.48. $C_{12}H_{22}ONI$. Calculated %: C 44.59; H 6.86; N 4.33; I 39.27.

2. 2-Methylene cyclopentanone. 27.3 g (0.085 mole) of the methiodide obtained in experiment 1 was dissolved in 75.5 ml of 10% $K_2CO_3$ solution (or 8.8% $NaHCO_3$ solution) and treated with 0.1 g of hydroquinone and 50 ml of ether; the mixture stood for 2 days at 20-25°. The ether layer was separated and the water solution was extracted with ether (twice with 30 ml). The combined ether extracts were washed with 0.1 N $H_2SO_4$ and water, dried with $CH_3COOK$, the ether distilled off, and the product vacuum-distilled (all these operations were carried out as quickly as possible). Yield 3.4 g (42%); b.p. 39° at 7 mm, $n^{20}D$ 1.4736 (cf. [7, 8]).

3. 4-(N-piperidylmethyl)-cyclopentanone-3-carboxylic acid hydrochloride (V) and the hydrochloride of the ethyl ester of this acid. A mixture of 89 g (0.7 mole) of cyclopentanone-3-carboxylic acid (IV) (for its preparation, see [1]), 42.2 g (0.35 mole) of piperidine hydrochloride, and 26.15 g of 40% formaldehyde (0.35 mole $CH_2O$) was heated 45 minutes on the boiling water bath. When it cooled, the reaction mass was dissolved in 20 ml of water and the unreacted starting acid (IV) was removed by ether extraction (44.5 g of acid was recovered). The water solution was freed from contaminants by extraction with chloroform (5 times with a total of 250 ml) and evaporated to dryness in a vacuum at 30-40°. The residue was dissolved in 20 ml of anhydrous alcohol, 150 ml of dry acetone was added and the mixture was allowed to stand at −10° for 2 days. The precipitate of hydrochloride was filtered, washed with a mixture of alcohol and acetone (1 : 7), then with ether, and was dried in a vacuum over $H_2SO_4$. The mother liquor was concentrated in a vacuum and in the manner described a further amount of hydrochloride was obtained. The total yield of hydrochloride (V) was 53.5 g (59%). After recrystallization from anhydrous alcohol the substance melted with decomposition at 143-144°.

Found %: C 55.51; H 7.39; N 5.46; Cl 13.61. $C_{12}H_{20}O_3NCl$. Calculated %: C 55.06; H 7.70; N 5.35; Cl 13.55.

A suspension of 9 g (0.034 mole) of the hydrochloride V in 100 ml of anhydrous alcohol was saturated at 0°

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* The ester of 3-cyclopentanone-1,2-dicarboxylic acid (XIII) itself did not react with formaldehyde and piperidine hydrochloride even under severe conditions.

with HCl (weight 67 g), upon which all the precipitate dissolved. The mixture remained overnight at 20-25° and then was evaporated to dryness in a vacuum at 30-35°. The residue was ground with acetone, filtered, washed with ether, and dried. Yield of ethyl4-(N-piperidylmethyl)-cyclopentanone-3-carboxylate hydrochloride was 9.3 g (93%); after recrystallization from anhydrous alcohol, it melted at 142-144° (decomposition).

Found %: C 57.81; H 7.88; N 4.85; Cl 12.38. $C_{14}H_{24}O_3NCl$. Calculated %: C 58.02; H 8.35; N 4.83; Cl 12.24.

4. Ethyl 4-(N-piperidylmethyl)-cyclopentanone-3-carboxylate methiodide (VI). A solution of 6 g (0.02 mole) of the ethyl ester hydrochloride of V in 8 ml of water was shken with 14 ml of 50% solution of $K_2CO_3$ and the base which formed was extracted with ether (8 times with a total of 200 ml). The ether solution was dried with $CH_3COOK$ and evaporated in a vacuum. The resulting ethyl4-(N-piperidylmethyl)-cyclopentanone-3-carboxylate, without preliminary distillation (the pure substance had a b.p. 104° at 0.3 mm, $n^{18.5}D$ 1.4818) was dissolved in 11 ml of dry acetone and 22 ml of anhydrous benzene, 25 g (0.176 mole) of methyl iodide was added, and the mixture stood overnight at 20-25°. The precipitate was filtered, washed with ether, and dried. Yield of methiodide (VI) was 7.6 g (93%); m.p. 123-125° (from anhydrous alcohol).

Found %: C 45.73; H 6.41; N 3.54; I 32.01. $C_{15}H_{26}O_3NI$. Calculated %: C 45.58; H 6.63; N 3.54; I 32.11.

5. Ethyl 4-methylenecyclopentanone-3-carboxylate (isosarcomycin ester) (VII). (a) Preparation. A solution of 5.7 g (0.015 mole) of methiodide VI and 11 ml of water was mixed with 29 ml of a 10% solution of $KHCO_3$ (0.03 mole), 0.1 g of hydroquinone and 25 ml of ether were added, and the mixture was allowed to stand for 2 days at 20-25°. The ether layer was separated and the water solution further extracted with ether (twice with 25 ml). The combined extracts were washed with 0.1 N $H_2SO_4$ and then with water, dried for 15 minutes with $CH_3COOK$, the ether was distilled off, and the residue vacuum distilled. The yield of ethyl ester of isosarcomycin (VII) was 1.1 g (45%); b.p. 69°, at 1 mm, $n^{20}D$ 1.4745.

Found %: C 63.85; H 7.16. $C_9H_{12}O_3$. Calculated %: C 64.27; H 7.19.

(b) Ozonolysis. A solution of 200 mg of the ethyl ester of isosarcomycin (VII) in 10 ml of dry ethyl acetate was ozonized at 0° until absorption of ozone stopped. The mixture was poured into a suspension of 300 mg of zinc dust in 10 ml of water, boiled on the water bath for 30 minutes and filtered hot into a solution of 300 mg of dimedon in 10 ml of alcohol, after which 20 ml of water was added. We obtained 80 mg of the dimedon derivative of formaldehyde with m.p. 189-190°.

(c) Hydrogenation and hydrolysis. A solution of 600 mg of the ethyl ester of isosarcomycin (VII) in 25 ml of alcohol was hydrogenated in the presence of 200 mg of skeletal nickel catalyst at normal pressure and room temperature until absorption of $H_2$ stopped (about 3 hours). The filtered solution was evaporated and the residue vacuum distilled. The yield of ethyl 4-methylcyclopentanone-3-carboxylate was 470 mg (77%); b.p. 63° at 1 mm, $n^{20}D$ 1.4530, $d^{20}_4$ 1.052.

Found %: C 63.11; H 8.79. $C_9H_{14}O_3$. Calculated %: C 63.51; H 8.29.

570 mg of the ethyl 4-methylcyclopentanone-3-carboxylate was boiled for 10 hours with 10 ml of 20% HCl, the solution decolorized with charcoal and evaporated in a vacuum. The residue (460 mg) gradually crystallized. The crystals were pressed on a porous plate and recrystallized from ether, m.p. 56-57.5°. The resulting acid gave a depression in a mixed melting point with racemic dihydrosarcomycin [1] but did not give a depression when mixed with 4-methylcyclopentane-3-carboxylic acid (XI) described in experiment 8.

Found %: C 58.60; H 6.60; $C_7H_{10}O_3$. Calculated %: C 59.14; H 7.09.

The semicarbazone of the isolated acid after recrystallization from 50% alcohol had m.p. 190-191° (decomposition) and gave no depression of melting point with the semicarbazone obtained in experiment 8.

Found %: C 48.31; H 6.47; N 20.90. $C_8H_{13}O_3N_3$. Calculated %: C 48.23; H 6.58; N 21.10.

6. Tetraester of pentane-1,2,2,4-tetracarboxylic acid (IX). To the sodium derivative obtained from 347 g (1.32 mole) of diethyl 3-carbomethoxybutane-1,1-dicarboxylate (VIII) [9] and 30.4 g (1.32 g-at.) of sodium in 400 ml of anhydrous alcohol 175 g (1.43 mole) of ethyl chloroacetate was slowly added with cooling. The reaction mixture was boiled for 1 hour, poured into 2 liters of water, and extracted with ether. The ether extract

was washed with a saturated solution of $NaHCO_3$, with water, and dried with $CaCl_2$. After vacuum distillation the yield of tetraester (IX) was 235 g (51%); b.p. 132-134° at 1.5 mm. The resulting ester was not entirely individual, because of partial transesterification of the carbomethoxy group during esterification. However, for the next step in the synthesis the substance was not further purified.

7. Triethyl 4-methylcyclopentanone-1,1,2-tricarboxylate (X). A mixture of 13.8 g (0.6 g-atom) of powdery sodium, 200 ml of anhydrous benzene, 2 ml of anhydrous alcohol, and 138 g (0.4 mole) of the tetraester IX were heated with stirring until a violent reaction began (about 70°), at which time the reaction mass had to be cooled. Then it was stirred for 3 hours at 95-100°, cooled, diluted with 200 ml of water and poured into a stirred mixture of 150 ml of concentrated HCl and 300 g of ice. The upper layer was separated, washed with a saturated solution of $NaHCO_3$ and with water, dried over $CaCl_2$, and evaporated. The residue was diluted with ether, quickly extracted twice with 600 ml of 5% NaOH solution, cooled to 0°, and the alkaline extract was quickly acidified with concentrated HCl, and the oil which precipitated was removed with ether. The ether solution was washed with a saturated solution of $NaHCO_3$, with water, and was dried over $CaCl_2$. The yield of ketoester X was 89 g (71%); b.p. 126° at 0.2 mm, $n^{17.5}D$ 1.4600.

Found %: C 57.12; H 6.93. $C_{15}H_{22}O_7$. Calculated %: C 57.31; H 7.06.

8. 4-Methylcylopentanone-3-carboxylic acid (XI). 89 g (0.28 mole) of ketoester X was boiled for 30 hours with 450 ml of 20% HCl, the solution was decolorized with charcoal, evaporated in a vacuum, and the residue distilled. Yield of XI 35 g (87%); b.p. 112-113° at 1 mm. The substance gradually crystallized, m.p. 57.5-59.5° (from ether).

Found %: C 58.75; H 7.00. $C_7H_{10}O_3$. Calculated %: C 59.14; H 7.09.

The semicarbazone of acid XI was recrystallized from 50% alcohol; m.p. 193-194° (decomposition) (cf.[5]).

Found %: C 48.65; H 6.51; N 21.25. $C_8H_{13}O_3N_3$. Calculated %: C 48.23; H 6.58; N 21.10.

9. Ethyl 4-methylcyclopentanone-3-carboxylate. 15 g (0.11 mole) of acid XI was boiled for 14 hours with 150 ml of anhydrous alcohol and 15 ml of concentrated $H_2SO_4$. The reaction mass was poured into 500 ml of water and extracted with ether. The extract was washed with 2 N $Na_2CO_3$ solution, with water, and was dried over $CaCl_2$. Yield 13.1 g (73%); b.p. 65° at 1 mm, $n^{20}D$ 1.4500, $d^{20}_4$ 1.057.

Found %: C 63.32; H 8.05. $C_9H_{14}O_3$. Calculated %: C 63.51; H 8.29.

10. 2-(N-Methylanilinomethylene)-cyclopentanone (XII). (a) Preparation. A mixture of 14.5 g (0.13 mole) of 2-oxymethylenecyclopentanone [10], 17.2 g (0.16 mole) of methylaniline, and 75 ml of anhydrous benzene were boiled with a Dean and Stark tube until water was no longer formed (about 1 hour). A precipitate separated from the reaction mixture when it was cooled; after concentration of the mother liquor a further amount of the substance was obtained. Yield 23.2 g (89%); m.p. 107-109° (from 40% alcohol).

Found %: C 77.70; H 7.64; N 6.98. $C_{13}H_{15}ON$. Calculated %: C 77.58; H 7.51; N 6.96.

(b) Attempts to introduce the N-piperidylmethyl group. A mixture of 5 g of 2-(N-methylanilinomethylene)--cylopentanone (XII), 3.2 g of piperidine hydrochloride, 2 g of 40% formaldehyde solution, and 20 ml of alcohol were heated 10 hours on a boiling water bath, and the strongly resinified reaction mass was then evaporated in a vacuum. Methylaniline was found in the distillate (identified as the acetyl derivative), and piperidine hydrochloride was isolated from the residue; no crystalline condensation product was found.

A mixture of 2 g of 2-(N-methylanilinomethylene)-cyclopentanone (XII) 0.85 g of piperidine, 0.45 g of paraformaldehyde, and 20 ml of anhydrous benzene were heated in a sealed tube at 100° for 21 hours, after which the reaction mixture was evaporated dry in a vacuum; only the starting compounds were isolated from the residue.

## SUMMARY

We have carried out the synthesis of an isomer of the anti-cancer antibiotic, sarcomycin. This isomer, called isosarcomycin, differs from the antibiotic in the position of the methylene group in the ring. Isosarcomycin has been obtained in the form of the ethyl ester, starting from cyclopentanone-3-carboxylic acid; condensation of the latter with formaldehyde and piperidine and then esterification and formation of the methiodide from the resulting compound led to the corresponding quaternary ammonium salt which split to synthesize the isosarcomycin ester.

## LITERATURE CITED

[1] M. M. Shemiakin, L. A. Shchukina and others, Zh. O. Kh. 27, 742 (1957).*

[2] H. Umezawa, T. Yamamoto and others, Antibiot. a. Chemother. 4, 514 (1954); I. R. Hooper, L. C. Cheney and others, Antibiot. a. Chemother. 5, 585 (1955).

[3] G. Büchi, N. C. Yang and others, Chem. a. Ind. 1063 (1953); J. Am. Chem. Soc. 77, 4401 (1955); E. E. van Tamelen, and S. R. Bach. J. Am. Chem. Soc. 77, 4683 (1955).

[4] W. B. Wheatley, C. T. Holdrege and L. Walsh J. Org. Ch. 21, 485 (1956).

[5] E. Hope and W. H. Perkin, J. Chem. Soc. 99, 762 (1911).

[6] C. Mannich and M. Bauroth, Ber. 57, 1108 (1924).

[7] C. Mannich and P. Schaller, Arch. Pharm. 276, 575 (1938).

[8] J. R. Nunn, and W. S. Rapson, J. Chem. Soc. 1949, 825.

[9] R. P. Evstigneeva, Disseration, The Synthesis of the Alkaloid Emetine, Moscow, 1950.**

[10] W. S. Johnson, and W. E. Shelberg, J. Am. Chem. Soc. 67, 1745 (1945).

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**In Russian.

# STUDIES IN THE FIELD OF COMPOUNDS WHICH CONTAIN THREE-MEMBERED OXYGEN RINGS

## XXII. THE REACTION OF GLYCIDIC ACID ESTERS WITH α- AND β-NAPHTHYLAMINES

V. F. Martynov and N. P. Sukhinin

In a series of previous studies [1-3] it was established that esters of β-monoalkyl and β-dialkylglycidic acids in reaction with aromatic amines of the aniline series opened the oxide ring on the side of the β-carbon atom. This work showed from a number of investigations the influence of steric hindrance, perhaps arising during the reaction, on the position at which the ring opened.

As the objects of study we used ethyl esters of the following glycidic acids: β-propyl, β,β-dimethyl, β-methyl, β-ethyl, β,β-tetramethylene, and β,β-pentamethyleneglycidic acids. As this list shows, all the glycidic acid esters have substituents in the β-position which differ in size. We chose the aromatic amines so that they would have the greatest possible difference from each other in filling the space around the amino group, but at the same time, so that there would be the least reactivity in the reaction of addition. The closest approach to this goal, it seemed to us, occurred with α- and β-naphthylamine.

The reaction of α- and β-naphthylamines with ethyl esters of glycidic acids took place in sealed glass tubes at 150-180°. When we opened the tubes, we almost always found some pressure. The clearest results in the reaction with β-naphthylamine were obtained for the ethyl ester of β,β-dimethylglycidic acid. The starting substances were taken in molar ratio to each other. They were heated at 170-180° for 10 hours. At the end of the reaction we found almost complete disappearance of the β-naphthylamine, and the reaction mixture had become very viscous. Analysis of the resulting substance for nitrogen showed that we had obtained the product of addition of β-naphthylamine to the oxide ring of glycidic acid. In the reaction of β-naphthylamine with the ethyl ester of β-propylglycidic acid (the reaction mixture was heated at 150-160° for 6 hours) we obtained a crystalline product whose analysis showed that in this case there was not only addition of β-naphthylamine to the oxide ring but at the same time, substitution of the ester group on the β-naphthylamine. Thus, it appears that the reactivities of the oxide ring and the ester group in respect to β-naphthylamine in the ethyl ester of β-propylglycidic acid are almost the same.

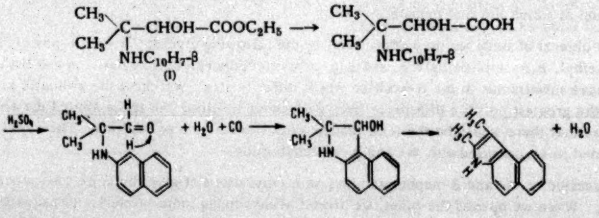
Exactly the same effect of substitution of the ester groups on naphthylamines were found in the reaction of β-naphthylamine with the ethyl esters of β-methyl, β-ethyl, and β,β-pentamethyleneglycidic acids. For these cases we did not succeed in isolating the products of reaction with one molecule of β-naphthylamine. It is interesting in this connection to observe that our earlier studies on the reaction of ethyl β,β-tetramethyleneglycidate with β-naphthylamine led to products of addition of only one molecule of naphthylamine on the oxide ring [4].

When we studied the reaction of the glycidates with α-naphthylamine the clearest results were also obtained with the ethyl ester of β,β-dimethylglycidic acid. In this case we succeeded in isolating the reaction product in a 32% yield. The substance was a very viscous yellowish liquid which did not crystallize even on long standing. The analysis for nitrogen and the observed molecular refraction showed that addition occurred on the oxide ring. Exactly the same addition of α-naphthylamine to the oxide ring occurred in the reaction with ethyl β,β-tetramethyleneglycidate. In this case the reaction product was isolated with a yield of 24% in the form of a hydrochloride. As to the addition of α-naphthylamine to ethyl β-propylglycidate, probably, in this case also, the reaction occurred in two directions; there was addition to the oxide ring and simultaneous substitution of the ester group. This was shown by the increased results of the analysis for nitrogen of the product obtained after one vacuum distillation. Therefore the yellowish, viscous reaction product was redistilled four times in a vacuum and we succeeded in obtaining a product, which, as the nitrogen analysis showed, was the result of addition of one molecule of α-naphthylamine to the oxide ring of the glycidate.

Thus, our experiments showed that the reactivity of α- and β-naphthylamines differ: β-naphthylamine reacted more easily with the ethyl glycidates than α-naphthylamine; in the reaction of β-naphthylamine with the glycidates the acid not only forms products of addition on the oxide ring, but also substitutes the ester group on the naphthylamine, which is shown to a lesser extent in α-naphthylamine. This difference in the behavior of these amines can probably be explained by steric hindrance which will be stronger in the reaction of α-naphthylamine, and also by differences in the basicity of these amines. Evidently, the basicity of α-naphthylamine will be less than that of β-naphthylamine because the ability to open the ring and to substitute the ester groups is more strongly expressed in β-naphthylamine.

To show the structure of the products obtained by addition we used the method consisting of their transformation under the action of sulfuric acid to the corresponding indoles [1-4].

When we heated the addition product of β-naphthylamine with ethyl β,β-dimethylglycidate with concentrated sulfuric acid at 110-120° we found a strong evolution of bubbles of carbon monoxide, with only slight darkening of the reaction mixture; tarring did not occur. This alone showed that β-naphthylamine added to the β-carbon atom of the ester. As a result of this reaction we should obtain the corresponding indole, whose formation could be expressed in the following way:



However, when we poured the reaction mixture on ice we did not find formation of a solid precipitate, as could be expected, since the resulting benzindole should not be soluble in water. Instead there was formed a small amount of an oily substance with a green color, which was a sulfonated derivative of benzindole. A water solution of this was treated with barium carbonate; the barium sulfate which formed and the unreacted barium carbonate were filtered off, and the filtrate was evaporated to small volume. After some time, glittering needles of the barium salt of the sulfobenzindole separated.

On the basis of these results, we can definitely say that in the reaction of β-naphthylamine with ethyl β,β-dimethylglycidate the oxide ring is opened on the side of the β-carbon atom, and as a result there is obtained the ethyl ester of α-hydroxy-β-(β-naphthylamino)-isovaleric acid (I).

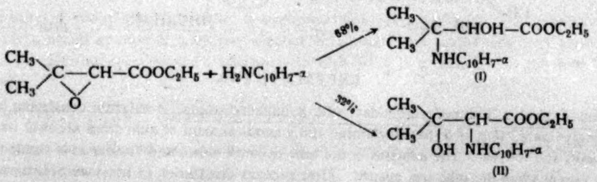
When the acid product obtained by reaction of ethyl β,β-dimethylglycidate with α-naphthylamine is treated with concentrated sulfuric acid, an entirely different result is obtained. When it is heated to 120° there is very rapid tarring with formation of a thick precipitate and a sharp odor of $SO_2$, which shows a deep decomposition of the product being studied. Such a result can be explained only by the fact that, as a result of reaction of α-naphthylamine with glycidates, the oxide ring is opened on the side of the α-carbon atom with formation of the ethyl ester of α-(α-naphthylamino)-β-hydroxyisovaleric acid (II). In this case, when concentrated sulfuric acid acts, there can really be tarring, because splitting out of a molecule of water occurs, with formation of an unsaturated amino-acid, which under the reaction conditions should give a tarry product. We found such tarring in the treatment by sulfuric acid of the product of addition of aromatic amines to esters of β-arylglycidic acids, which showed that they had the structure of α-arylamino-β-hydroxyacids [5]. However, the evolution of some quantity of gas led us to the opinion that there might have been present in the starting product another isomer with a hydroxyl group in the α-position. In this connection we raised the question of determining the percent content of isomers in the starting product. For a solution of this problem we used different ratios of both isomers to cconcentrated sulfuric acid.

From a consideration of the structures of both possible isomers, I and II, it is clear that when sulfuric acid acts, only one of them, with the hydroxyl group in the α-position, will be decomposed with evolution of carbon monoxide. Hence, a determination of carbon monoxide permits us to estimate the amount of the isomer in the starting product.

For quantitative determination of carbon monoxide we used the method applied in the analysis of fatty acids [6] with only the difference that the reaction mixture was heated not on the open flame, but in a sulfuric acid bath at 120°.

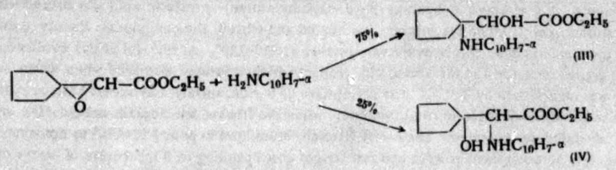
We must say that we had already hoped to use such a method to show the structure of the products obtained in the reaction of aniline with the ethyl ether of β-methyl-β-ethylglycidic acid [3]. Analysis showed that the reaction went only in one direction toward formation of α-hydroxy-β-amino acid. For a supplementary test of this method, we studied product (I) for which transformation into benzindole established the structure as ethyl α-hydroxy-β-(β-naphthylamino)-isovalerate. Quantitative determination of carbon monoxide showed that the reaction went 100% in one direction.

When the addition product of α-naphthylamine to ethyl β,β-dimethylglycidate was treated with concentrated sulfuric acid, only 68% of the total possible carbon monoxide was evolved. Hence we can conclude that the missing 32% CO belongs to the second isomer which is present. Thus, the reaction in this case proceeds in both possible directions



When the product of addition of α-naphthylamine and ethyl β,β-tetramethyleneglycidate is mixed with sulfuric acid, we find heavy tar formation, appearance of a carbonaceous residue, and strong odor of $SO_2$. It is important to remember that we earlier studied the reaction of ethyl β,β-tetramethyleneglycidate with β-naphthylamine and found that the reaction product with sulfuric acid gave the corresponding benzindole without any tarring [4].

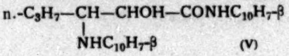
Hence, the reaction of ethyl β,β-tetramethyleneglycidate with α-naphthylamine also goes in two directions with formation of the ethyl ester of α-hydroxy-β-(β-naphthylamino)-β,β-tetramethylenepropionic acid (III) and the ethyl ester of α-(β-naphthylamino)-β-hydroxy-β,β-tetramethylenepropionic acid (IV). Quantitative determination of carbon monoxide shows that only 75% of the theoretically possible CO is evolved.



The addition product of α-naphthylamine to ethyl β-propylglycidate reacts with sulfuric acid and undergoes almost the same tarring, which positively indicates that in this case both possible isomers are formed. However, unfortunately, because of lack of material, we could not determine the carbon monoxide quantitatively.

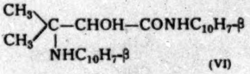
Thus, our investigations have shown that the opening of the oxide ring in β-mono- and dialkyl substituted glycidates under the action of aromatic amines can proceed not only on the β-, but also on the carbon atom of the α-side. The latter reaction occurs when there is considerable steric hindrance in the attack on the β-carbon atom.

As to the products formed in the reaction of β-naphthylamine with ethyl esters of β-propyl-, β-methyl, β-ethyl, and β,β-pentamethylene glycidic acids, here there occurs not only addition of β-naphthylamine to the oxide ring but simultaneous substitution of the ester group on the naphthylamine. Such compounds, as we have shown, are very stable to sulfuric acid [7, 8] and splitting of carbon monoxide in this case occurs at very high temperatures, at which the rest of the molecule begins to decompose. Therefore we did not run special experiments to determine their structures. However, our earlier studies showed that aniline and p-toluidine added to the β-carbon atom of these glycidates [1, 2, 9]. One of the preceding experiments [4] and this work show that aniline and β-naphthylamine have about the same activity with respect to the glycidates and both add to the β-atom. In this connection, we are fully justified in ascribing to the reaction product of β-naphthylamine with these esters the formula of naphthylamides of α-hydroxy-β-amino acids, namely: α-hydroxy-β-(β-naphthylamino)-caproic acid naphthylamide (V), α-hydroxy-β-(β-naphthylamino)-(β-methyl)-valeric acid naphthylamide (VI), and α-hydroxy-β-(β-naphthylamino)-β,β-pentamethylenepropionic acid naphthylamide (VII).

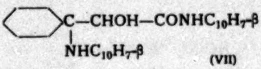


$$n.\text{-}C_3H_7\text{—}\underset{\displaystyle NHC_{10}H_7\text{-}\beta}{\underset{|}{CH}}\text{—}CHOH\text{—}CONHC_{10}H_7\text{-}\beta$$

(V)



(VI)



(VII)

## EXPERIMENTAL

Reaction of ethyl β,β-dimethylglycidate with β-naphthylamine. A mixture consisting of 18 g of ethyl β,β-dimethylglycidate, 18 g of β-naphthylamine and a small amount of anhydrous alcohol was heated in a sealed tube for 10 hours at 170-180°. The contents of the tube became brown and viscous as a result of heating; some pressure was present when the tube was opened. After vacuum distillation (1 mm) we obtained a yellowish, very viscous liquid which crystallized after some time. After recrystallization from ligroin, the substance melted at 71-72°. The yield was 20 g (54%).

Found %: N 4.90. $C_{17}H_{21}O_3N$. Calculated %: N 4.87.

To determine carbon monoxide we used the method described in the literature [6]. The reaction mixture was heated to 120° on a sulfuric acid bath with constant stirring by a mechanical stirrer; the reaction mixture then became only slightly colored. Heating was continued until evolution of bubbles of carbon monoxide completely stopped; the gas was collected over 50% KOH.

Found %: CO 9.80. $C_{17}H_{21}O_3N$. Calculated %: CO 9.76.

Conversion of ethyl α-hydroxy-β-(β-naphthylamino)-isocaproate into the barium salt of 2,3-dimethylsulfobenzindole. 1 g of ethyl α-hydroxy-β-(β-naphthylamino)-isovaleric acid was mixed with 4 ml of concentrated sulfuric acid. When the mixture was heated and stirred, the components dissolved and at 95° evolution of carbon monoxide began; this became very intense at 110-120°. At the end of gas evolution, the brownish liquid was poured onto ice and the green, oily product which separated dissolved when water was added. The sulfuric acid was neutralized by $BaCO_3$. The precipitate of barium sulfate and excess barium carbonate was filtered off, the filtrate was evaporated to small volume. When the filtrate was cooled, needle-like crystals of the barium salt of sulfobenzindole separated. They were filtered, dried, and kept at 110-115° to constant weight; the crystals then changed to an amorphous powder and lost weight corresponding to 9 molecules of water of crystallization. We obtained 0.3 g (25%).

Found %: N 4.15; Ba 19.8. $C_{28}H_{24}O_6N_2S_2Ba$. Calculated %: N 4.1; Ba 20.0.

The reaction of ethyl β,β-dimethylglycidate with α-naphthylamine. A mixture consisting of 15.5 g of ethyl β,β-dimethylglycidate, 15.4 g of α-naphthylamine, and a small amount of anhydrous alcohol was heated in a sealed tube for 10 hours at 170-180°. The reaction mixture became yellow and very viscous. After 2 vacuum distillations we obtained 10 g (32%) of a yellow, viscous liquid which did not crystallize even on long standing.

B. p. 164° (0.5 mm) $n^{20}D$ 1.591, $d^{20}_4$ 1.140, $MR_D$ 84.589; calc. 80.762.

Found %: N 4.95. $C_{17}H_{23}O_3N$. Calculated %: N 4.87.

Carbon monoxide was determined by the above method. When the substance was mixed with concentrated sulfuric acid, much tar was found even with slight heating.

Found %: CO 6.62. $C_{17}H_{21}O_3N$. Calculated %: CO 9.75.

Reaction of ethyl β,β-tetramethyleneglycidate with α-naphthylamine. A mixture consisting of 17 g of ethyl β,β-tetramethyleneglycidate, 14 g of α-naphthylamine, and a small amount of anhydrous alcohol was heated in a sealed tube for 10 hours at 170-180°. The reaction mixture became brown and very viscous. The unreacted starting product was distilled off in a vacuum and the residue in the flask was dissolved in anhydrous alcohol and a stream of dry HCl was passed through the solution. The hydrochloride which precipitated was filtered on a Buchner funnel and washed with absolute ether. Yield 8.4 g (24%).

Found %: N 4.10. $C_{19}H_{24}O_3NCl$. Calculated %: N 4.00.

In the quantitative determination of carbon monoxide when the substance reacted with concentrated sulfuric acid, much tar was formed.

Found %: CO 6. $C_{19}H_{24}O_3NCl$. Calculated %: CO 8.02.

Reaction of ethyl β-propylglycidate with α-naphthylamine. 10.7 g of ethyl β-propylglycidate, 10 g of α-napthylamine and a small amount of anhydrous alcohol were heated in a sealed tube for 6 hours at 160-170°. After four vacuum distillations we obtained a viscous, yellowish liquid (b.p. 174-176° at 0.5 mm) in the amount of 3 g, $n^{20}D$ 1.5948.

Found %: N 4.73. $C_{18}H_{23}O_3N$. Calculated %: N 4.70.

In the attempt to obtain the corresponding indole by treatment of the product with concentrated sulfuric acid, we found tar formation.

Reaction of ethyl-β-propylglycidate with β-naphthylamine. 10 g of ethyl β-propylglycidate, 10 g of β-naphthylamine, and a small amount of anhydrous alcohol were heated in a sealed tube for 6 hours at 150-160°. With vacuum distillation (0.5 mm) we isolated 5 g of a yellow, viscous product which after some time partly crystallized. It was recrystallized from petroleum ether. M. p. 82-83°

Found %: N 7.18. $C_{26}H_{26}O_2N_2$. Calculated %: N 7.20.

Reaction of ethyl β-methyl-β-ethylglycidate with β-naphthylamine. 15.3 g of ethyl β-methyl-β-ethylglycidate, 13.6 g of β-napthylamine and a small amount of anhydrous alcohol were heated in a sealed tube at 170-180° for 10 hours. After vacuum distillation (184-187° at 0.5 mm) the substance crystallized. After recrystallization from petroleum ether it melted at 83-84° (decomposition).

Resulting in 3 g (10.5%).

Found %: N 7.27. $C_{26}H_{26}O_2N_2$. Calculated %: N 7.20.

Reaction of ethyl β,β-pentamethyleneglycidate with β-naphthylamine. 24 g of ethyl β,β-pentamethyleneglycidate, 19 g of β-naphthylamine, and a small amount of anhydrous alcohol were heated 13 hours in a sealed tube at 170-190°. After vacuum distillation, the substance crystallized. After recrystallization from petroleum ether it melted at 77-78° (decomposition). We obtained 9 g (15%).

Found %: N 6.68. $C_{28}H_{28}O_2N_2$. Calculated %: N 6.60.

## SUMMARY

1. We have studied the reaction of α- and β-naphthylamines with a series of esters of glycidic acids. We showed that β-naphthylamine is the more reactive substance.

2. We have established that in the reaction of β-naphthylamine with ethyl β,β-dimethylglycidate the

oxide ring is opened on the side of the $\beta$-carbon atom. The resulting addition product under the action of concentrated sulfuric acid can be converted to the corresponding indole.

3. We have established that $\alpha$-naphthylamine reacts with ethyl $\beta,\beta$-dimethyl and $\beta,\beta$-tetramethyleneglycidate to form a mixture of two isomers. In this case the oxide ring is opened on the sides both of the $\beta$- and the $\alpha$-carbon atoms.

## LITERATURE CITED

[1] V. F. Martynov and G. Ol'man, Zh. O. Kh. 25, 1561 (1955).*

[2] V. F. Martynov, Zh. O. Kh. 23, 1659 (1953).*

[3] V. F. Martynov and Ia. A. Kastron, Zh. O. Kh. 23, 1559 (1953).*

[4] V. F. Martynov, Zh. O. Kh. 27, 1191 (1957).*

[5] V. F. Martynov and G. Ol'an, Zh. O. Kh. 27, 1881 (1957).*

[6] G. Maier, Analysis and Determination of the Structure of Organic Substances, ONTI 371 (1935).

[7] V. F. Martynov, Zh. O. Kh. 23, 1654 (1953).*

[8] V. F. Martynov, Zh. D. Vasiutina, and L. P. Nikulina, Zh. O. Kh. 26, 1405 (1956).*

[9] V. F. Martynov, Zh. O. Kh. 23, 2006 (1953).*

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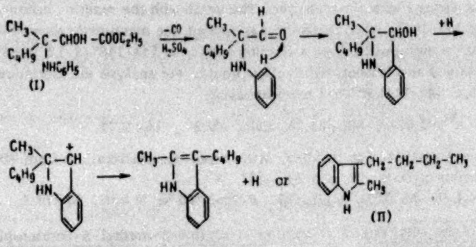
# STUDIES IN THE FIELD OF COMPOUNDS WHICH CONTAIN THREE-MEMBERED OXYGEN RINGS

## XXIII. THE REACTION OF ETHYL ESTERS OF β-METHYL-β-BUTYL-, AND β-METHYL-β-PHENYL-GLYCIDIC ACIDS WITH ANILINE

V. F. Martynov and Ia. A. Kastron

In a previous communication [1] we described the reaction of aromatic amines with ethyl esters of glycidic acids which had the same substituents on the β-carbon atom. The present work is a continuation of this study. The ethyl ester of β-methyl-β-butylglycidic acid is described for the first time. It was obtained by the method of Darzans with a 42% yield. The addition of aniline to the ethyl ester of this glycidic acid was carried out with considerable difficulty because of the steric hindrance of the substituents on the β-carbon atom. Actually, heating for 16 hours of a mixture of aniline and the ethyl glycidate at 160-170° did not give the desired result; addition of aniline to the oxide ring did not occur. Then the reaction mixture was placed in a steel bomb which was heated in an oil thermostat for 36 hours at 175-180°. Under these conditions, reaction occurred and the addition product was obtained in 43% yield. It was a very viscous liquid which crystallized after some time, but we could not measure all the characteristic constants of the liquid substance.

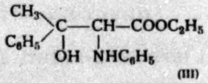
On the basis of previous work [1] we could assume that we had obtained the ethyl ester of α-hydroxy-β-anilino-β-methyl-β-butylpropionic acid (I). However, final evidence could only be the conversion of this product into the corresponding indole. For this purpose the compound was treated with hot, concentrated sulfuric acid. As a result of this reaction, we observed evolution of carbon monoxide and from the reaction mixture we obtained the expected indole. Thus it was finally shown that in the reaction of aniline with ethyl β-methyl-β-butylglycidate, the oxide ring was opened on the side of the β-carbon atom.



To show the structure of the resulting indole we synthesized 2-methyl-3-butylindole by the method of A. E. Arbuzov from methyl amyl ketone. The picrates obtained from the two indoles had the same melting point and their mixture gave no depression.

Thus, as the result of the reaction we obtained 2-methyl-3-butylindole (II), that is, a retropinacoline rearrangement which occurred during the reaction and proceeded very selectively, producing a shift of the heavier butyl groups.

From the point of view of studying the retropinacoline rearrangement in indole synthesis, there is a positive interest in obtaining the ethyl ester of α-hydroxy-β-anilino-β-methyl-β-phenylpropionic acid. This compound could be obtained by addition of aniline to the ethyl ester of β-methyl-β-phenylglycidic acid. We carried out this reaction and obtained a crystalline product which according to the analysis was the product of addition to the oxide ring of the glycidate of one molecule of aniline. When concentrated sulfuric acid acted on this compound, much tar was formed with comparatively slight heating and no indole could be isolated. This fact could only be explained by the opening of the oxide ring on the side of the α-carbon atom when aniline reacted with ethyl β-methyl-β-phenylglycidate, and as a result the formation of the ethyl ester of α-anilino-β-hydroxy-β-methyl-β-phenylpropionic acid (III) took place.



$$\mathrm{(CH_3)(C_6H_5)C(OH)-CH(NHC_6H_5)-COOC_2H_5}$$

(III)

In this case, the action of sulfuric acid should give an unsaturated amino acid which under these conditions would be converted to a tarrry product. This assumption was the more probable because we had found in the case of ethyl-β-phenylglycidate that aniline added to the α-carbon atom [2]. Further, the product which we obtained could be separated by fractional crystallization into two compounds, exactly the same in composition, but with different crystal form and melting points. One of them, less soluble in ethyl alcohol, was isolated in the form of needles with m.p. 114-115°. The other, more soluble, was isolated from the mother liquors in the form of warty crystals with m.p. 88-89°. These two crystalline forms are evidently diastereoisomers, since the ethyl ester of α-anilino-β-hydroxy-β-methyl-β-phenylpropionic acid contains two asymmetric carbon atoms. Both crystalline forms under the influence of sulfuric acid form much tar, which shows that they have entirely analogous structures.

## EXPERIMENTAL

Synthesis of the ethyl ester of β-methyl-β-butylglycidic acid was carried out by the method of Darzans. To a mixture of 100 g (1 mole) of freshly distilled methylbutyl ketone, 122 g (1 mole) of ethyl monochloroacetate and 500 ml of dry ether was added, in small portions with energetic stirring, 1 mole of sodium ethylate. Addition of sodium ethylate was carried out at such a rate that the temperature of the reaction mixture did not rise above +3°. On the second day, after the usual process of treatment, we obtained 78 g (42%) of ester:

B.p. 61-63° at 0.5-1 mm, $d^{20}_4$ 0.9640, $n^{20}D$ 1.4326, $MR_D$ 50.17; calc. 49.48; $EM_D$ 0.69.

Found %: C 64.45; H 9.99. $C_{10}H_{18}O_3$. Calculated %: C 64.48; H 9.74.

Synthesis of the ethyl ester of α-hydroxy-β-anilino-β-methyl-β-butylpropionic acid (I). 74.4 g (0.4 mole) of the ethyl ester of β-methyl-β-butylglycidic acid and 111.6 g (1.2 mole) of freshly distilled aniline were placed in a steel bomb, connected with a manometer. The bomb with the reaction mixture was heated in an oil thermostat for 36 hours at 175-180°. When the bomb was opened, the manometer showed a pressure of 3.5 atm. The reaction mixture was vacuum distilled and a fraction boiling at 144-148° (1-1.5 mm) was collected. We obtained 48 g (43%) of the ester I as a viscous, light yellow liquid. For analysis the substance was twice fractionated and the fraction with b.p. 142-144° at 0.5-1 mm was taken:

$d^{20}_4$ 1.0438, $n^{20}D$ 1.5248, $MR_D$ 81.98, calc. 79.27, $EM_D$ 2.71.

The substance crystallized on standing. After three recrystallizations from 80% ethyl alcohol it was obtained as transparent colorless crystals with m.p. 80.5-81°

Found %: N 4.88. M 270.2. $C_{16}H_{25}O_3N$. Calculated %: N 5.01. M 279.3.

Conversion of the ethyl ester of α-hydroxy-β-anilino-β-methyl-β-butylpropionic acid into 2-methyl-3-butylindole. 4.1 g of the ethyl ester I was mixed with 26 ml of concentrated sulfuric acid. The reaction mixture was carefully heated on an oil bath. At 80° evolution of carbon monoxide began. The most intense evolution of gas occurred at 90-95° (thermometer in the reaction mixture). Reaction lasted about 3 hours without evident tar formation. At the end of the gas evolution the reaction mixture was poured onto ice and was neutralized with a cold aqueous solution of NaOH. The indole was extracted with ether and after vacuum distillation was obtained as a thick, light yellow liquid with b.p. 124-127° at 1 mm, becoming red in air. The yield of 2-methyl-3-butylindole was 1.5 g (55.5%).

$d^{20}_4$ 0.9944, $n^{20}D$ 1.5671, $MR_D$ 61.52; calc. 57.86, $EM_D$ 3.62.

Found %: N 7.67. $C_{13}H_{17}N$. Calculated %: N 7.48.

A picrate was obtained from the synthesized indole. When hot alcoholic solutions of molar amounts of both components were mixed we obtained cherry red needles with m.p. 133° (in a sealed capillary). Recrystallization did not change the melting point.

For identification, 2-methyl-3-butylindole (II) was synthesized from methyl amyl ketone by the method of A. E. Arbuzov ($MR_D$ 62.72, $EM_D$ 4.8). The picrate was in the form of cherry red needles with m.p. 133-134° (in a sealed capillary). The mixed melting point of both picrates showed no depression.

Reaction of the ethyl ester of β-methyl-β-phenylglycidic acid with aniline. For the reaction we used the ethyl β-methyl-β-phenylglycidate obtained by the method of Darzans, b.p. 107-111° at 2 mm:

$d^{20}_4$ 1.0442, $n^{20}D$ 1.5182, $MR_D$ 56.63; calc. 55.12, $EM_D$ 1.51.

30 g of ethyl β-methyl-β-phenylglycidate and 42 g of aniline were heated in Wood's metal in a flask with a reflux condenser to which was joined a Tishchenko flask with sulfuric acid. Heating was continued for 14 hours with weak boiling of the reaction mixture. In the vacuum distillation we collected the fraction with b.p. 156-180° at 2 mm. The product was a light yellow liquid which crystallized after three days. Yield about 45%. We should remark that after the distillation, a considerable amount of heavy, tarry liquid remained in the flask and was not investigated.

The resulting product was repeatedly recrystallized from 96% ethyl alcohol. As a result, we isolated two forms of crystals which differed in melting point and crystal shape. One substance, which separated from a still warm alcohol solution as colorless needles had m.p. 114-115°

Found %: C 72.21; H 7.25; N 4.94. M 308.0. $C_{18}H_{21}O_3N$. Calculated %: C 72.22; H 7.07; N 4.67. M 299.3.

The other substance, which crystallized from the mother liquors as fine, warty crystals had m.p. 88-89°.

Found %: C 72.53; H 7.46; N 4.87. M 287.6. $C_{18}H_{21}O_3N$. Calculated %: C 72.22; H 7.07; N 4.67. M 299.3.

Both crystal forms under the action of concentrated sulfuric acid gave much tar without evident separation of any gas. The mixture of both substances melted at 83-85°

## SUMMARY

1. We have studied the reaction of the ethyl esters of β-methyl-β-butyl- and β-methyl-β-phenylglycidic acids with aniline.

2. We have established that the oxide ring of ethyl β-methyl-β-butylglycidate is opened by aniline on the side of the β-carbon atom. The oxide ring of ethyl β-methyl-β-phenylglycidate was also opened, probably, on the side of the α-carbon atom.

3. We carried out the conversion of the ethyl ester of α-hydroxy-β-anilino-β-butylglycidic acid to 2-methyl-3-butylindole.

## LITERATURE CITED

[1] V. F. Martynov and Ia. A. Kastron, Zh. O. Kh. 23, 1559 (1953);* Zh. O. Kh. 24, 498 (1954);* Zh. O. Kh. 26, 63 (1956).*

[2] V. F. Martynov and G. Ol'man, Zh. O. Kh. 27, 1881 (1957).*

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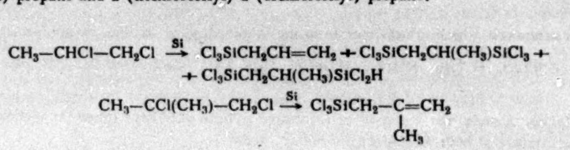
# THE BEHAVIOR OF SOME DICHLOROALKANES AND DICHLOROALKENES IN CONDITIONS OF DIRECT SYNTHESIS

A. D. Petrov, G. I. Nikishin, and N. P. Smetankina

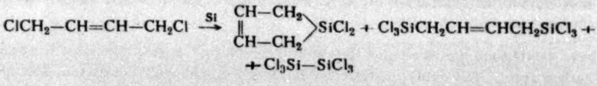
In the reaction of dichloroethane [1] and 1,2-dichloropropane [2] with silicon, only disilanes were observed among the reaction products, along with silicochloroform and silicon tetrachloride. In the case of 1,4-dichlorobutane [3] and 1,2-dichloro-3-butene [4], as we have shown, along with the disilanes there is also formation of cyclic monosilanes with a silicon atom in a five-membered ring. In the present work we have chosen as the object of study close homologs of dichloroethane, which had not been sufficiently investigated earlier [2], 1,2-dichloropropane, and 1,2-dichloro-2-methylpropane, and also the isomers of 1,2-dichloro-3-butene; 1,4-dichloro-2-butene and 3-chloro-2-(chloromethyl)-1-propene. It was shown that under the conditions of the synthesis, 1,2-dichloropropane and 1,2-dichloro-2-methylpropane easily lose hydrogen chloride with conversion to the corresponding allyl chloride and methylallyl chloride. From these in turn by reaction with silicon are formed allyltrichlorosilane and methylallyltrichlorosilane. In the case of 1,2-dichloropropane we obtained the previously unidentified disilanes, 1,2-bis-(trichlorsilyl)-propane and 1-(trichlorosilyl)-2-(dichlorosilyl)-propane.



$$CH_3{-}CHCl{-}CH_2Cl \xrightarrow{Si} Cl_3SiCH_2CH{=}CH_2 + Cl_3SiCH_2CH(CH_3)SiCl_3 + Cl_3SiCH_2CH(CH_3)SiCl_2H$$

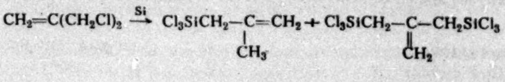
$$CH_3{-}CCl(CH_3){-}CH_2Cl \xrightarrow{Si} Cl_3SiCH_2{-}\underset{\displaystyle CH_3}{\underset{|}{C}}{=}CH_2$$

The reaction of 1,4-dichloro-2-butene with silicon proceeds in accordance with the scheme:



$$ClCH_2{-}CH{=}CH{-}CH_2Cl \xrightarrow{Si} \text{(CH=CH)(CH}_2)_2\text{SiCl}_2 + Cl_3SiCH_2CH{=}CHCH_2SiCl_3 + Cl_3Si{-}SiCl_3$$

It is interesting that there is only 6% 1,1-dichloro-1-(3-silacyclopentene) in the reaction mixture, while in the reaction mixture obtained in the reaction of 1,2-dichloro-3-butene with silicon its content is 15% [4]. Evidently in the earlier case reaction proceeds through the stage of 1,4-dichloro-2-butene, but at the moment of its formation, which explains the higher yield. The formation of hexachlorodisilane from the dichloride under the conditions of direct synthesis had not been observed and was unexpected for us. It structure was confirmed by conversion to hexamethyldisilane and by spectrum analysis of the latter. Attempts to carry out closing of a four-membered ring in the reaction of 3-chloro-2-(chloromethyl)-1-propene with silicon were unsuccessful. The sole identified products were methylallyltrichlorosilane and 3-(trichlorosilyl)-2-(trichlorosilylmethyl)-1-propene.



$$CH_2{=}C(CH_2Cl)_2 \xrightarrow{Si} Cl_3SiCH_2{-}\underset{\displaystyle CH_3}{\underset{|}{C}}{=}CH_2 + Cl_3SiCH_2{-}\underset{\displaystyle CH_2}{\underset{\|}{C}}{-}CH_2SiCl_3$$

Attempts to replace a chlorine atom in the latter product by a methyl group using methylmagnesium chloride caused splitting at the Si−C bond and we could isolate only hexamethyldisiloxane. A similar interesting anomaly was earlier found only in the methylation of methylallyltrichlorosilane by an excess of methylmagnesium chloride [5]. We also studied the behavior of vinylidene chloride under the conditions of direct synthesis. In the temperature range up to 450° the chief mass of vinylidene chloride did not undergo any change in contact with a copper-silicon alloy. There was only the formation of a small amount of silicochloroform and silicon tetrachloride. We also isolated several grams of a high-boiling liquid whose properties corresponded to those of 1,1-bis-(trichlorosilyl)-ethene. However, we did not succeed in making a detailed study because of the difficulty of obtaining this substance in large amounts.

## EXPERIMENTAL

A glass tube 700 mm long and 40 mm in diameter was filled with pieces of copper-silicon alloy and placed in a tubular electric oven; nitrogen was blown through it and at a temperature of 300 ± 10° the dichloride under study was passed through. The reaction products were condensed by a water condenser. The reaction mixture was distilled in a column 1 meter high, filled with glass rings with a diameter of 3 mm. The isolated fractions were repeatedly distilled in a column with an effectiveness of 25 theoretical plates. In the Table we give the rate of passing the dichloride and the yield of condensate in separate experiments.

TABLE

| No. of experiment | Dichloride studied | Passed (in g) | Rate (g/ hour) | Amount of condensate |
|---|---|---|---|---|
| I | $CH_3-CHCl-CH_2Cl$ | 555 | 21 | 277 |
| II | $CH_3-CCl(CH_3)-CH_2Cl$ | 565 | 24.5 | 385 |
| III | $ClCH_2-CH=CH-CH_2Cl$ | 650 | 26 | 400 |
| IV | $CH_2=C(CH_2Cl)_2$ | 820 | 18.5 | 650 |

Experiment I. From the condensate we isolated: silicochloroform 68.3 g (24.6%), silicon tetrachloride 60 g (21.7%); allyltrichlorosilane 20 g (7.2%) with b.p. 115-117° (752 mm), $n^{20}D$ 1.4422, $d^{20}_4$ 1.2132, $MR_D$ 38.30; calc. 38.96 (literature data [6]; b.p. 116-118°, $n^{18}D$ 1.4455). 1-(Trichlorosilyl)-2-dichlorosilylpropane 6.6 g (2.3%) with b.p. 192-195° (764 mm), $n^{20}D$ 1.4663, $d^{20}_4$ 1.3385, $MR_D$ 57.25; calc. 56.84.

Found %: Si 20.96. $C_3H_7Si_2Cl_5$. Calculated %: Si 20.31.

1,2-Bis-(trichlorosilyl)-propane 39 g (14%) with b.p. 212-214° (762 mm), $n^{20}D$ 1.4809, $d^{20}_4$ 1.4479, $MR_D$ 61.11; calc. 60.84.

Found %: C 12.35; H 1.81; Si 18.02. $C_3H_6Si_2Cl_6$. Calculated %: C 11.57; H 1.93; Si 18.00.

The literature gives only the boiling point of this compound, obtained by direct synthesis with a yield of 1.6% [2].

In the reaction of 1,2-bis-(trichlorosilyl)-propane with excess methylmagnesium chloride we obtained a 20% yield of 1,2-bis-(trimethylsilyl)-propane with b.p. 167°, $n^{20}D$ 1.4296, $d^{20}_4$ 0.7725, $MR_D$ 62.97; calc. 63.06.

Found %: C 57.17; H 12.76; Si 29.90. $C_9H_{24}Si_2$. Calculated %: C 57.35; H 12.84; Si 29.81.

Experiment II. From the condensate we isolated: silicochloroform 33.5 g (8.7%), silicon tetrachloride 139 g (36%), methylallyl chloride 26 g (6.8%) with b.p. 67-69° (748 mm), $n^{20}D$ 1.4280, $d^{20}_4$ 0.9260 (literature data [7]: b.p. 71.5° (760 mm), $n^{20}D$ 1.4291, $d^{20}_4$ 0.9269); methylallyltrichlorosilane 56.5 g (14.7%) with b.p. 138.0° at 730 mm, $n^{20}D$ 1.4542 (literature data [5]: b.p. 139° at 743 mm, $n^{20}D$ 1.4533).

In the reaction of methylallyltrichlorosilane with an equivalent amount of methylmagnesium chloride we obtained 52.5% methylallyltrimethylsilane with b.p. 109° (726.5 mm), $n^{20}D$ 1.4203, $d^{20}_4$ 0.7380. The combination scattering spectrum corresponded to that given in the literature [8] (literature data [5]: b.p. 111-111.5° at 758 mm, $n^{20}D$ 1.4193, $d^{20}_4$ 0.7397).

Experiment III. In the condensate we found: silicochloroform 40 g (10%), silicon tetrachloride 66.6 g (16.7%);

24 g (6%) of 1,1-dichloro-1-(3-silacyclopentene) with b.p. 134-136° (741 mm), $n^{20}D$ 1.4780 (literature data [4]: b.p. 135° at 753 mm, $n^{20}D$ 1.4782).

Found %: C 31.12; H 3.75. $C_4H_6SiCl_2$. Calculated %: C 31.37; H 3.95.

Hexachlorodisilane 23.5 g (6%) with b.p. 145-146° (741 mm), $n^{20}D$ 1.4701 (literature data [9]: b.p. 144-148°); 1,4-bis-(trichlorosilyl)-butene 29 g (7.3%) with b.p. 240-243°, $n^{20}D$ 1.4859 (literature data [4]: b.p. 243°, $n^{20}D$ 1.4879).

Found %: Si 17.54. $C_4H_6Si_2Cl_6$. Calculated %: Si 17.39.

From 1,1-dichloro-1-(3-silacyclopentene) by methylation with methylmagnesium chloride we obtained 65% of 1,1-dimethyl-1-(3-silacyclopentene) with b.p. 101.5° (746 mm), $n^{20}D$ 1.4424, $d^{20}_4$ 0.8062 (literature data [4] b.p. 100.5-101° at 741 mm, $n^{20}D$ 1.4433, $d^{20}_4$ .8067).

In an analogous way we obtained from hexachlorodisilane, hexamethyldisilane with b.p. 111-111.5°, $n^{20}D$ 1.4214, $d^{20}_4$ 0.7293, $MR_D$ 50.84; calc. 51.07 (literature data [10]: b.p. 113-114° at 760 mm, $n^{20}D$ 1.4229, $d^{20}_4$ 0.7268).

In the reaction of 1,4-bis-(trichlorosilyl)-2-butene with methylmagnesium chloride we obtained 1,4-bis-(trimethylsilyl)-2-butene (yield 48.5%) with b.p. 190° (753 mm); $n^{20}D$ 1.4385, $d^{20}_4$ 0.7799 (literature data [4]: b.p. 187.5-188.5°, $n^{20}D$ 1.4398, $d^{20}_4$ 0.7789).

Experiment IV. From the condensate we isolated: silicochloroform 62 g (9.5%), silicon tetrachloride 74 g (11.3%); methylallyltrichlorosilane 76.5 g (11.5%) with b.p. 185-139°, $n^{20}D$ 1.4570; 3-(trichlorosilyl)-2-(trichlorosilylmethyl)-1-propene 49 g (7.5%) with b.p. 239-240° (722 mm), $n^{20}D$ 1.4931, $d^{20}_4$ 1.4052, $MR_D$ 66.81; calc. 65.00.

Found %: Si 18.05. $C_4H_6Si_2Cl_6$. Calculated %: Si 17.39.

From methylallytrichlorosilane and methylmagnesium chloride we obtained methylallyltrimethylsilane (yield 40.6%) with b.p. 110° (731 mm), $n^{20}D$ 1.4202, $d^{20}_4$ 0.7384. Its combination scattering spectrum fully agreed with that given in the literature [7].

In the action of excess methylmagnesium chloride on 1-(trichlorosilyl)-2-(trichlorosilymethyl)-2-propene along with substitution of chlorine atoms by methyl groups there was rupture of a Si−C bond. As a result we obtained only hexamethyldisiloxane (yield 50%) with b.p. 99-100°, $n^{20}D$ 1.3777, $d^{20}_4$ 0.7633 (literature data [11]: b.p. 99-100°, $n^{20}D$ 1.3771, $d^{20}_4$ 0.7638).

From the reaction mixture obtained by passage through a tube with a Cu−Si alloy of 650 g of vinylidene chloride at 450°, we isolated only 9 g of 1,1-bis-(trichlorosilyl)-ethene (besides $HSiCl_3$ and $SiCl_4$), with b.p. 109° (51 mm), $n^{20}D$ 1.4861, $d^{20}_4$ 1.4939, $MR_D$ 56.67; calc. 55.74.

Found %: Si 18.71. $C_2H_2Si_2Cl_2$. Calculated %: Si 19.03.

## SUMMARY

1. We have established that 1,2-dichloropropane and 1,2-dichloro-2-methylpropane under the conditions of direct synthesis easily lose hydrogen chloride and are converted to allyl chloride and methylallyl chloride. In the case of 1,2-dichloro-2-methylpropane, the methylallyltrichlorosilane is the sole reaction product; in the case of 1,2-dichloropropane, besides the allyltrichlorosilane, disilanes are also formed.

2. In the reaction of 1,4-dichloro-2-butene with silicon, along with disilanes is found formation of a cyclic monosilane, 1,1-dichloro-1-(3-silacyclopentene).

3. The reaction products of 3-chloro-2-(chloromethyl)-1-propene with silicon were methylallyltrichlorosilane and 3-(trichlorosilyl)-2-(trichlorosilylmethyl)-1-propene; the later reacts with $CH_3MgCl$ with splitting of a Si−C bond.

## LITERATURE CITED

[1] W. Patnodc and R. Schiessler, US Pat. 2381000, 2381002; Ch. A. 39, 4889 (1945).

[2] W. D. English, A. Maurins and R. V. Nicholls, Canad. J. Chem. 30, 646 (1952).

[3] A. D. Petrov, N. P. Smetankina, and G. I. Nikishin, Izv. AN SSSR, OKhN 1958, 147.

[4] A. D. Petrov, G. I. Nikishin, N. P. Smetankina and Iu. P. Egorov, Izv. AN SSSR, OKhN 1955, 947.

[5] A. D. Petrov and G. I. Nikishin, Izv. AN SSSR, OKhN 1956, 243.

[6] V. A. Ponomarenko and V. F. Mironov, Izv. AN SSSR, OKhN 1954, 497.

[7] B. A. Kazanskii and M. Iu. Lukina, Izv. AN SSSR, OKhN 1951, 47.

[8] A. D. Petrov, Iu. P. Egorov, V. F. Mironov, G. I. Nikishin, and A. A. Bugorkova, Izv. AN SSSR, OKhN 1956, 50.

[9] C. Friedel and A. Ladenburg, Lieb. Ann. 203; 241 (1880).

[10] M. G. Voronkov and Iu. I. Khudobin, Zh. O. Kh. 26, 584 (1956).

[11] B. O. Pray, L. H. Sommer, G. M. Goldberg, G. T. Kerr, P. A. Di Giorgio and F.C. Whitmore, J. Am. Chem. Soc., 70, 932 (1948).

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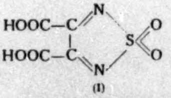
# STUDIES IN THE FIELD OF THE CHEMISTRY OF 2,1,3-THIODIAZOLE

## VIII. THE OXIDATION OF BENZO-2,1,3-THIODIAZOLE AND ITS DERIVATIVES

V. G. Pesin, A. M. Khaletskii, and Chou Ch'in

In a previous study, two of us showed that benzo-2,1,3-thiodiazole and its derivatives, and also naphtho-2,1,3-thiodiazole [1, 2] along with their aromatic properties are definitely unsaturated; the unsaturated character of these compounds however does not exclude a definite specificity. Thus, some reactions characteristic of ethylene compounds do not occur with benzo-2,1,3-thiodiazole (addition of HCl, diene synthesis). Also, it is found that the unsaturation shown for benzo-2,1,3-thiodiazole and its derivatives is weakened in the 4,7-dichloro derivative while the aromatic character of the latter is strengthened. In this connection, is is interesting to study further the unsaturated properties of benzo-2,1,3-thiodiazole and its derivatives and for this purpose we have used oxidation.

In the oxidation of benzo-2,1,3-thiodiazole, its 5-methyl-, 5-chloro-, and 4,7-dichloro derivatives by peracetic acid we find destruction of all the organic part of the molecule (the sulfur is found only in the form of ammonium sulfate). In the oxidation of 5-chlorobenzo-2,1,3-thiodiazole besides ammonium sulfate was isolated a slight amount of the 2,4-dinitrophenylhydrazone of glycolic aldehyde (presumed), and in the oxidation of benzo-2,1,3-thiodiazole was obtained only qualitative evidence of the presence of an aldehyde group. It is interesting to note in this connection that when 5-methylbenzo-2,1,3-thiodiazole is heated with 30% hydrogen peroxide in glacial acetic acid, no notable change is found [3]; also there is no change in the action of perbenzoic acid on benzo-2,1,3-thiodiazole in chloroform at 0°. In the oxidation of benzo-2,1,3-thiodiazole by potassium permanganate we isolated two products; one, judging by analytical data and ability to form a dimethylallyl derivative, is preferably S-dioxy 2,1,3-thiodiazole-4,5-dicarboxylic acid (I), the other was not more closely investigated, but the analytical data agree with the composition $C_2H_2N_2O_4SK_2$ and its structure can be assumed to be represented by formula (II).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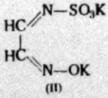
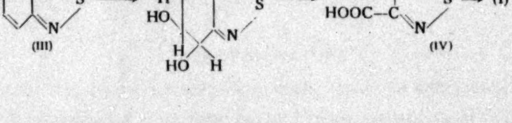
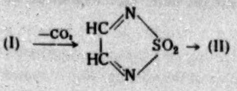

(II)

The formation of these substances can be explained if it is assumed that oxidation by potassium permanganate goes through preliminary addition of the elements of hydrogen peroxide (according to Wagner); the 2,1,3-thiodiazole-4,5-dicarboxylic acid which is formed is further oxidized to the S-dioxide (I)



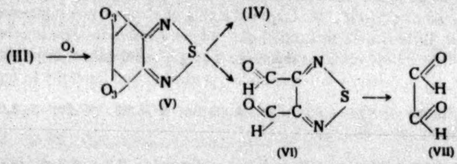
Simultaneously there is transformation of the S-dioxide (I) according to the scheme



The oxidation of 2-methylbenzo- and 1',2'-naphthothiodiazole go in the same way.

This theory of the mechanism of oxidation of benzo-2,1,3-thiodiazole by potassium permanganate can be confirmed by the oxidation of 4,7-dichlorobenzo-2,1,3-thiodiazole which is much "less unsaturated" than the previous one; this also is found in halogenation. While benzo-2,1,3-thiodiazole easily adds chlorine and bromine, 4,7-dichlorobenzo-2,1,3-thiodiazole does not add halogens. In the oxidation of 4,7-dichlorobenzo-2,1,3-thiodiazole by potassium permanganate, reaction goes less energetically than in the oxidation of benzo-2,1,3-thiodiazole, and so it must be carried out under stronger conditions.

In ozonization of benzo-2,1,3-thiodiazole (III), an ozonide (V) is isolated with m.p. 60°,[*] which after decomposition gives a mixture of 2,1,3-thiodiazole-4,5-dicarboxylic acid (IV), 2,1,3-thiodiazole-4,5-dialdehyde (VI), and glyoxal (VII); in this case the reaction mechanism can be given as follows:



The last two substances were isolated in the form of the corresponding semicarbazones; some quantity of ammonium sulfate was also obtained. On the basis of these data, the oxidation of benzo-2,1,3-thiodiazole and some of its derivatives by potassium permanganate and ozone indicates that thiodiazole has an unsaturated character, as was earlier established in studies of the halogenation reactions.

## EXPERIMENTAL

*Oxidation of benzo-2,1,3-thiodiazole by peracetic acid.* 10 g of III and 135 ml of acetic acid which contained 11% peracetic acid were heated on the boiling water bath for 48 hours, after which the reaction mass was diluted with water. The precipitate which separated (1.3 g of benzo-2,1,3-thiodiazole which did not react) was filtered off, and the filtrate was concentrated (a considerable amount of benzo-2,1,3-thiodiazole was then precipitated) and the residue was washed with alcohol and ether; we obtained 0.75 g of ammonium sulfate.

Found %: S 23.75, 23.98. $(NH_4)_2SO_4$. Calculated %: S 24.24.

After evaporation of the alcohol-ether filtrate we obtained a thick liquid which reduced Fehling's solution but from which we could not isolate individual substances.

*Oxidation of benzo-2,1,3-thiodiazole by perbenzoic acid.* 1 g of III was dissolved in 15 ml of chloroform and to the solution at 0° was added 42.6 ml of a chloroform solution of perbenzoic acid (containing 2.6 g of perbenzoic acid). On the next day, after distillation of the solvent, the residue was treated with 10% sodium hydroxide solution; after drying it melted at 40-42°. A mixed melting point with the starting benzo-2,1,3-thiodiazole gave no depression.

*Oxidation of 5-methylbenzo-2,1,3-thiodiazole by peracetic acid.* To a solution of 5 g of substance, 50 ml of 93% acetic acid, and 50 ml of acetic anhydride at 60° was gradually added through a dropping funnel 50 ml of 30% hydrogen peroxide. After heating for two days to 60° and diluting the solution with water, we obtained 2.8 g of starting substance. After distillation of the filtrate in a vacuum and treatment of the residue with alcohol and ether, we obtained ammonium sulfate (no other substance could be isolated).

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[*] We express thanks to A. I. Iakubchik and N. G. Kasatkina for valuable aid and advice in carrying out the ozonolysis at the Leningrad State University.

Oxidation of 4,7-dichlorobenzo-2,1,3-thiodiazole by peracetic acid. 5 g of the substance and 140 ml of 11% peracetic acid were submitted to heating on a boiling water bath for 3 days, and then the acetic acid solution was diluted with water; we obtained 1.5 g of the starting substance, and, when the filtrate was treated as before, 0.95 g of ammonium sulfate.

Oxidation of 5-chlorobenzo-2,1,3-thiodiazole with peracetic acid. 1.5 g of substance and 60 ml of 11% peracetic acid were heated on the boiling water bath for 2 days, after which the acetic acid solution was diluted with water and gave 0.15 g of starting substance; when the filtrate was treated as before it gave 0.17 g of ammonium sulfate. From the alcohol solution after removal of the $(NH_4)_2SO_4$, the action of 2,4-dinitrophenylhydrazine gave 0.13 g of a 2,4-dinitrophenylhydrazone which after recrystallization from a mixture of ethyl acetate and alcohol (1 : 1) melted at 177.5-179.5°.

Found %: C 40.55, 40.16; H 3.48, 3.44; N 23.19, 23.78. $C_8H_8O_5N_4$. Calculated %: C 40.00; H 3.33; N. 23.33.

Oxidation of benzo-2,1,3-thiodiazole by potassium permanganate. To a mixture of 4 g of III and 40 ml of water was added gradually with stirring at 50°, 30 g of potassium permanganate as an 8% solution (to a faint rose color). The manganese dioxide which separated was filtered, washed with hot water, and the combined filtrates were concentrated in a vacuum at 50-60°. We obtained 2.42 g of a crystalline substance which contained potassium, was easily soluble in water, little soluble in alcohol, and did not dissolve in organic solvents. From the filtrate (after neutralization with hydrochloric acid) was separated 2.86 g of a substance, m.p. 268° (with decomposition) which after recrystallization from water was little soluble in alcohol and insoluble in organic solvents.

Found %: C 23.70, 23.39; H 1.11, 0.86; N 13.62, 13.68; S 15.23, 15.20. $C_4H_2O_6N_2S$. Calculated %: C 23.30; H 0.97; N 13.59; S 15.52.

Silver salt of S-dioxy 2,1,3-thiodiazole-4,5-dicarboxylic acid. 0.3 g of S-dioxy-2,1,3-thiodiazole-4,5-dicarboxylic acid was dissolved in 10 ml of 10% ammonia solution, the solution was evaporated on the water bath to remove ammonia, the residue was dissolved in water, and to the filtrate was added a 20% solution of silver nitrate. The precipitate was separated, washed with water and dried at 95° to give 0.6 g of salt.

Found %: Ag 51.80, 51.77. $C_4O_6N_2SAg_2$. Calculated %: Ag 51.43.

Analysis of the substance which contained potassium.

Found %: C 10.79; 10.66; H 1.01; 1.19; N 12.12, 12.18. $C_2H_2O_4N_2SK_2$; Calculated %: C 10.53; H 0.89; N 12.28.

Oxidation of 5-methylbenzo-2,1,3-thiodiazole by potassium permanganate. 1 g of substance was heated with 10 ml of water at 50° and with constant stirring a solution of 4.4 g of potassium permanganate in 250 ml of water was added. The mixture was boiled for 10 minutes. Manganese dioxide was filtered off and water was distilled from the filtrate to a minimum volume. When hydrochloric acid was added, 0.46 g (33.6%) of needles separated, with m.p. 263-264°. A mixed melting point with S-dioxy-2,1,3-thiodiazole-4,5-dicarboxylic acid gave no depression.

Oxidation of 4,7-dichlorobenzo-2,1,3-thiodiazole by potassium permanganate. A mixture of 3 g of the substance and 40 ml of 4% sodium hydroxide solution was heated to boiling and at this temperature a solution of 20 g of potassium permanganate in 250 ml of water was added gradually with stirring to a weak rose color. After separation of the manganese dioxide and concentration of the filtrate in a vacuum, we isolated 2.32 g (70%) of the oxidation product.

Found %: C 10.96, 10.61; H 1.12, 1.05; N 11.93, 12.04. $C_2H_2O_4N_2SK_2$. Calculated %: C 10.53; H 0.887; N 12.28.

Oxidation of 1',2'-naphtho-2,1,3-thiodiazole by potassium permanganate. a) 1.5 g of substance was heated with 20 ml of water to 85-90° and at this temperature a solution of 20 g of potassium permanganate in 400 ml of water was added gradually with stirring. After 20 minute boiling and separation of the manganese dioxide, the filtrate was concentrated in a vacuum; we obtained 0.37 g of substance (20%).

Found %: C 10.66, 10.61; H 1.07, 0.97; N 11.82, 12.00. $C_2H_2O_4N_2SK_2$. Calculated %: C 10.53; H 0.887; N 12.28.

b) A mixture of 1.5 g of 1',2'-naphtho-2,1,3-thiodiazole and 100 ml of water was heated to 50-60°, and at this temperature with constant stirring was gradually added 4 g of potassium permanganate, after which the reaction mixture was cooled and the manganese dioxide was filtered off. After neutralization of hydrochloric acid, the filtrate was concentrated in a vacuum to 10 ml, treated with alcohol, and the potassium chloride which separated was filtered off. The alcohol-water filtrate was concentrated in a vacuum to minimum volume; 0.17 g of crystals with m.p. 268-272° (with decomposition) separated. A mixed melting point with S-dioxy 2,1,3-thiodiazole-4,5-dicarboxylic acid obtained by the oxidation of benzo-2,1,3-thiodiazole by potassium permanganate gave no depression.

Ozonization of benzo-2,1,3-thiodiazole. Ozone (concentration of ozone ~ 7%) was passed into a solution of 4 g of III in 65 ml of chloroform at −10° to −15°; we isolated 5 g of a substance (m.p. 60° with decomposition in a sealed tube; yield 73.2%). This yellowish powder with an unpleasant odor was kept at −5°; at higher temperatures (15-20°) it was converted into a yellow mass.

1.45 g of the ozonide was dissolved in water, the solution was neutralized with barium carbonate, the precipitate (barium sulfate with excess barium carbonate) was filtered off, washed with hot water, and the combined filtrates concentrated at 50° in a vacuum. The resulting white precipitate was filtered and recrystallized from water; we obtained 0.5 g of the barium salt of 2,1,3-thiodiazole-4,5-dicarboxylic acid.

Found %: C 15.77, 15.48. $C_4O_4N_2SBa$. Calculated %: C 15.55.

When the water solution of the barium salt was treated with concentrated sulfuric acid, the precipitate separated, and the filtrate concentrated, we obtained a substance which, after drying at 80°, melted at 172-173°.

Found %: N 15.73, 15.90. $C_4H_2O_4N_2S$. Calculated %: N 16.09.

The solution after separation of the barium salt of 2,1,3-thiodiazole-4,5-dicarboxylic acid was diluted with a mixture of alcohol and water (1 : 1) and treated with semicarbazide solution to give a semicarbazone with m.p. 193-195° (66.6%); after recrystallization from a mixture of alcohol and water, m.p. 195.5-197°.

Found %: C 28.09; 28.21; H 3.23, 3.31; N 43.73, 43.41; S 12.40, 12.75. $C_6H_8O_2N_8S$. Calculated %: C 28.13; H 3.12; N 43.75; S 12.50.

According to the analytical data this corresponds to the semicarbazone of 2,1,3-thiodiazole-4,5-dialdehyde.

Investigation of the decomposition products of the ozonide of benzo-2,1,3-thiodiazole was carried out further as follows: the water solution obtained after decomposition of 6.4 g of ozonide was vacuum-distilled and the residue in the form of a thick liquid crystallized after treatment with alcohol and ether; we obtained 0.28 g of a substance which decomposed at 340°. It was soluble in water, insoluble in ether, did not darken when heated in the flame of a burner, its water solution evolved ammonia when it was boiled with a sodium hydroxide solution, and it gave a precipitate with barium chloride; thus it was shown that it was ammonium sulfate.

The alcohol-ether solution after removal of ammonium sulfate was diluted with water, neutralized with barium carbonate, and the insoluble barium salts were filtered off. After the filtrate had been concentrated in a vacuum and the further portion of barium salt which separated had been removed, we isolated 3.45 g of semicarbazone. This was a mixture of the semicarbazones of 2,1,3-thiodiazole-4,5-dialdehyde and glyoxal. These semicarbazones were separated by their different solubilities in alcohol; while the semicarbazone of 2,1,3-thiodiazole-4,5-dialdehyde was comparatively easily soluble in alcohol, glyoxal semicarbazone was insoluble and melted above 270°.

Found %: C 28.39, 28.58; H 4.84, 4.59. $C_4H_8O_2N_6$. Calculated %: C 27.99; H 4.65.

## SUMMARY

1. In the oxidation of benzo-2,1,3-thiodiazole, its 5-methyl-, 5-chloro-, and 4,7-dichloro derivatives by peracetic acid, there is decomposition of all the organic portion of the molecules: the final products of the reaction are chiefly ammonium sulfate and small amounts of carbonyl compounds.

2. Benzo-2,1,3-thiodiazole and also 5-methylbenzo-2,1,3-thiodiazole are oxidized by potassium permanganate (at 50°) with the formation of S-dioxy 2,1,3-thiodiazole-4,5-dicarboxylic acid and a product with the composition $C_2H_2O_4N_2SK_2$. 4,7-Dichlorobenzo-2,1,3-thiodiazole under these conditions reacts weakly with potassium permanganate (at 100°) with the formation preferably of the substance $C_2H_2O_4N_2K_2$.

3. 1',2'-Naphtho-2,1,3-thiodiazole reacts with potassium permanganate, depending on the reaction conditions, to form either the product $C_2H_2O_4N_2SK_2$, or a mixture of this with S-dioxy 2,1,3-thiodiazole-4,5-dicarboxylic acid.

4. Benzo-2,1,3-thiodiazole is oxidized by ozone with the formation of ammonium sulfate, 1,2,3-thiodiazole-4,5-dicarboxylic acid, 1,2,3-thiodiazole-4,5-dialdehyde, and glyoxal.

## LITERATURE CITED

[1] A. M. Khaletskii, V. G. Pesin, and Chao Chih-chung, DAN SSSR 106, 88 (1956).

[2] Chao Chih-chung, Dissertation, Studies in the Field of Synthesis of Benzo-2,1,3-thiodiazole Derivatives, Leningrad (1956).

[3] O. Hinsberg, Ber. 48, 1611 (1915).

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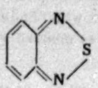
# CHEMISTRY OF 2,1,3-THIADIAZOLE

## IX. REACTION OF o-BENZOQUINONE DIOXIME WITH SULFUR DICHLORIDE

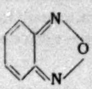
V. G. Pesin, A. M. Khaletskii and Chou Ch'in

The synthesis of 2,1,3-benzothiadiazole (I) and its derivatives and a study of the substitution, addition and oxidation reactions of the latter [1] revealed that together with a well-defined aromatic character, the indicated heterocycle shows some unsaturation. However, this heterocycle does not lend itself to certain reactions characteristic of unsaturated compounds, like, for example, the diene synthesis. In addition, it was found that the unsaturated properties of (I) become weaker in some of its derivatives, and in contrast, the aromatic character is enhanced. Studies employing physical methods (measurement of interatomic distances [2], determination of dipole moments [3]) also fail to yield an answer as to the structure of (I) and its derivatives. In connection with the above, we undertook the synthesis of 2,1,3-benzothiadiazole from compounds whose quinoid structure was not in doubt.

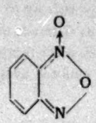
According to the literature [4], benzofurazan (II) does not react with phosphorus pentasulfide; it seemed to us that the oxygen in the diazole ring of benzofuroxan (III) is less firmly bound to the nitrogen atoms than it is in benzofurazan (II).



(I)



(II)



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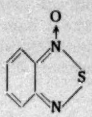
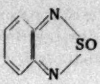


(IV)



(V)

Proceeding from this, we attempted to synthesize (I) or its oxide (IV) from benzofuroxan (III) by reacting the latter with either phosphorus pentasulfide or hydrogen sulfide, but in neither case did we succeed (the same as in our earlier attempts to synthesize 2,1,3-benzothiadiazole from o-benzoquinone dioxime and phosphorus pentasulfide).

Negative results were also obtained when we attempted to react o-benzoquinone dioxime with hydrogen sulfide in the presence of sodium acetate; in both cases benzofurazan (II) was obtained instead of (I), i.e. dehydration occurred.

The obtained results led us to postulate that the possiblity of forming the thiadiazole ring is not excluded when compounds, capable of reacting under mild conditions (at low temperature), avoiding dehydration, are reacted with o-benzoquinone dioxime. Based on such considerations, we investigated the reaction of o-benzoquinone dioxime with thionyl chloride, sulfinylaniline and sulfur dichloride. As our investigations revealed, thionyl chloride and sulfinylaniline do not react with o-benzoquinone dioxime; the 2,1,3-benzothiadiazole derivative was obtained only when o-benzoquinone dioxime was reacted with sulfur dichloride. The reaction product can be assigned either structure (IV) or (V).

## EXPERIMENTAL

Benzofuroxan (III) [5]. A solution of 32.2 g of o-nitroaniline in 250 ml of methyl alcohol, in the presence of 8.8 g of sodium hydroxide, was oxidized with 275 ml of 16.45% sodium hypochlorite solution. The red reaction mass soon deposited a yellow precipitate, which after filtration, washing with water, and drying had m.p. 64-68°; the yield was 31 g (97.69%).

Reaction of benzofuroxan with phosphorus pentasulfide. A mixture of 0.7 g of benzofuroxan and 1.4 g of phosphorus pentasulfide in 20 ml of benzene was heated under reflux with constant stirring. After refluxing for 2 hours the insoluble precipitate was filtered and dried at 40°; after recrystallization from dilute alcohol, m.p. 64-65°. The mixed melting point with benzofuroxan was not depressed.

Reaction of benzofuroxan with hydrogen sulfide. Hydrogen sulfide was passed into a solution of 0.5 g of benzofuroxan in a mixture of 25 ml of alcohol and 2.5 g of 50% sodium acetate solution. After 30 minutes the liberated sulfur was filtered, and the alcohol solution was evaporated at 40° to dryness, in which connection an individual compound could not be isolated from the black-green residue.

o-Benzoquinone dioxime [5]. A solution of 37 g of hydroxylamine hydrochloride in 75 ml of water was added to a solution of 24.7 g of benzofuroxan in 360 ml of methyl alcohol, and then the reaction mixture was heated on the water bath for 30 minutes at 50°. After cooling to room temperature, 30% sodium hydroxide solution was added from a dropping funnel until nitrogen evolution ceased. The sodium chloride was filtered, the filtrate was diluted with 500 ml of water, then acidified with acetic acid, the yellow precipitate suction-filtered, washed with water, then precipitated from ammonia solution with hydrochloric acid (d 1.04), and finally recrystallized from alcohol. We obtained 13.2 g of o-benzoquinone dioxime with m.p. 144° (with decompn.); yield 52.67%.

Reaction of o-benzoquinone dioxime with thionyl chloride. Thionyl chloride (1 ml) was added in drops and with stirring to a suspension of 0.5 g of the dioxime in 50 ml of benzene. After stirring for 1 hour the mixture was filtered and the filtrate was evaporated in the air to dryness. The residue after recrystallization from dilute alcohol had m.p. 41-44°. The mixed melting point with authentic benzofurazan was not depressed.

Reaction of o-benzoquinone dioxime with sulfinylaniline. Sulfinylaniline (1 ml) was added in drops and with constant stirring to a solution of the dioxime in 20 ml of anhydrous alcohol. After heating on the boiling water bath for 10 minutes the alcohol solution was evaporated to dryness and the residue was treated with dilute hydrochloric acid (d 1.04); the obtained precipitate had m.p. 41-44°. The mixed melting point with authentic benzofurazan was not depressed.

Reaction of o-benzoquinone dioxime with sulfur dichloride. A solution of 1 ml of sulfur dichloride in 5 ml of benzene was added in drops and with constant stirring to a suspension of 1 g of the dioxime in 20 ml of dry benzene at room temperature. The mixture was filtered, the benzene filtrate evaporated, and the residue dried. We obtained 0.7 g of compound (63.57%), which after recrystallization from water had m.p. 81-83°. The compound was obtained as slender yellow needles, which evolved hydrogen sulfide when reduced with zinc dust in the presence of dilute hydrochloric acid.

Found %: C 47.78, 48.14; H 2.65, 2.72; N 18.13, 18.47; S 21.00, 21.16. $C_6H_4ON_2S$. Calculated %: C 48.00; H 2.66; N 18.67; S 21.34.

## SUMMARY

1. The possibility of synthesizing 2,1,3-benzothiadiazole derivatives by the reaction of either benzofuroxan or o-benzoquinone dioxime with phosphorus pentasulfide, and also with hydrogen sulfide, was investigated; here it was established that benzofuroxan does not react with the indicated compounds, while o-benzoquinone dioxime is converted to benzofurazan.

2. The behavior of thionyl chloride, sulfinylaniline and sulfur dichloride toward o-benzoquinone dioxime was investigated, and here it was found that the first two promote dehydration (benzofurazan is formed); the reaction of o-benzoquinone dioxime with sulfur dichloride yields 2,1,3-benzothiadiazole oxide.

## LITERATURE CITED

[1] A. M. Khaletskii and V. G. Pesin, J. Gen. Chem. 20, 1914 (1950);* 24, 133 (1954);* A. M. Khaletskii, V. G. Pesin and Chao Chih-Chung, Proc. Acad. Sci. USSR 106, 88 (1956); 113, 627 (1957);* V. G Pesin, A. M. Khaletskii and Chao Chih-Chung, J. Gen. Chem. 27, 1575 (1957).*

[2] V. Luzzati, Acta cryst. 4, 193 (1951).

[3] R. W. Hill and L. E. Sutton, J. chim. phys. 46, 244 (1944).

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*Original Russian pagination. See C.B. translation.

[4] O. Hinsberg, Ber. 22, 2895 (1899).

[5] L. G. Green and F. W. Rowe, J. Chem. Soc. 1912, 2452.

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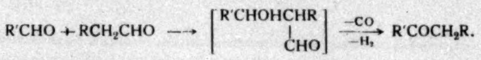
# CATALYTIC PREPARATION OF KETONES FROM A MIXTURE OF n-BUTYRIC ACID AND ETHYL ALCOHOL

G. V. Golodnikov, B. N. Dolgov and L. N. Propp

In a previous paper [1] we reported that the passage of a mixture of acetic acid and n-butyl alcohol over Cr–Mn catalyst yields methyl propyl ketone, and together with it, the symmetrical ketones, acetone and dipropyl ketone. The scheme proposed by us for the reaction postulated decomposition of the initially formed ester (butyl acetate) to aldehydes, followed by aldol condensation of the latter, and subsequent transformation of the aldol to methyl propyl ketone.

The present paper is a continuation of our studies on the synthesis of mixed ketones from mixtures of acids and alcohols. As the study subject in the present case we selected a mixture of ethyl alcohol and n-butyric acid. This mixture is interesting for the reason that ethyl butyrate, postulated as being the intermediate product in the present ketonization, is metameric with butyl acetate, postulated as being the intermediate product in the ketonization of a mixture of acetic acid and n-butyl alcohol. Subsequent transformations of the indicated metameric esters should lead to obtaining the same aldehydes, namely acetaldehyde and butyraldehyde. Consequently, the observed formation of the same ketones as the result of reaction, i.e. of methyl propyl ketone, acetone and dipropyl ketone, confirms to a certain degree the validity of the proposed mechanism for the ketonization of mixtures of acid and primary alcohols. The formation of a mixed ketone proceeds by the following scheme:

$$RCH_2COOH + R'CH_2OH \xrightarrow{-H_2O} RCH_2COOCH_2R' \underset{<T}{\overset{>T}{\rightleftarrows}} R'CHO + RCH_2CHO,$$



$$R'CHO + RCH_2CHO \longrightarrow \left[\begin{array}{r} R'CHOHCHR \\ | \\ CHO \end{array}\right] \xrightarrow[-H_2]{-CO} R'COCH_2R.$$

For a mixture of ethyl alcohol and n-butanoic acid, $R = C_2H_5$ and $R' = CH_3$. For a mixture of acetic acid and n-butyl alcohol, $R = H$ and $R' = C_3H_7$.

The experiments with a mixture of n-butyric acid and ethyl alcohol were run in the presence of additional hydrogen, added in a mole ratio of 1 : 1 on the mixture. The experimental conditions and results are given in Tables 1-3. The following conditions proved to be most favorable for the methyl propyl ketone yield (21.7%): temperature 420°, space velocity 80, and component ratio in the mixture 1 : 1. An increase in the amounts of esters and butyraldehyde with increase in the space velocity to 160 is evidence that the time of contact is too short to permit further transformations, i.e. decomposition of the ester to aldehydes and subsequent condensation of the aldehydes.

A preponderance of n-butyric acid in the mixture leads to increasing the yield of dipropyl ketone, while increasing the amount of ethyl alcohol causes some increase in the yield of acetone.

A substantial reduction in the yield of methyl propyl ketone is observed when the hydrogen is omitted (Table 1, Expt. 7). Here the yield of dipropyl ketone remained practically unchanged, since the ketonic decomposition of acids and oxide catalysts does not require the additional introduction of hydrogen.

The total yield of ketones under the optimum conditions was 52.3% on the weight of starting mixture (Table 1, Expt. 6).

### TABLE 1

Experiment Conditions: Space Velocity 80, Mole Ratio of Ethyl Alcohol and n-Butyric Acid 1 : 1

| Expt. No. | Temperature | Yield (in % on starting mixture) | | | | |
|---|---|---|---|---|---|---|
| | | acetone | methyl propyl ketone | dipropyl ketone | esters | butyraldehyde |
| 1 | 250° | 0.0 | 0.0 | 5.8 | 25.6 | 0.0 |
| 2 | 300 | 0.0 | 0.0 | 12.3 | 41.2 | 1.6 |
| 3 | 350 | 0.0 | 0.0 | 16.6 | 34.0 | 1.0 |
| 4 | 380 | 0.0 | 0.0 | 16.9 | 26.1 | 0.9 |
| 5 | 400 | 0.0 | 7.4 | 22.2 | 23.0 | 0.8 |
| 6 | 420 | 1.9 | 21.7 | 28.7 | 6.9 | 0.0 |
| 7 | 420 | 4.0 | 14.3 | 27.0 | 2.2 | 0.0 |
| 8 | 440 | 3.3 | 20.5 | 24.7 | 2.9 | 0.0 |
| 9 | 460 | 4.3 | 17.3 | 22.2 | 0.0 | 0.0 |
| 10 | 480 | 3.1 | 12.4 | 19.0 | 0.0 | 0.0 |

### TABLE 2

Experiment Conditions: Temperature 420°, Mole Ratio of Ethyl Alcohol and n-Butyric Acid 1 : 1

| Space velocity | Yield (in % on starting mixture) | | | | |
|---|---|---|---|---|---|
| | acetone | methyl propyl ketone | dipropyl ketone | esters | butyraldehyde |
| 40 | 4.3 | 20.5 | 25.9 | 6.1 | 0.9 |
| 80 | 1.9 | 21.7 | 28.7 | 6.9 | 0.0 |
| 120 | 1.3 | 15.7 | 31.9 | 11.7 | 0.0 |
| 160 | 0.0 | 11.4 | 27.8 | 17.7 | 7.5 |

### TABLE 3

Experiment Conditions: Temperature 420°, Space Velocity 80

| Mole ratio of n-butyric acid and ethyl alcohol in mixture | Yield (in % on starting mixture) | | | | |
|---|---|---|---|---|---|
| | acetone | methyl propyl ketone | dipropyl ketone | esters | butyraldehyde |
| 2 : 1 | 1.7 | 13.5 | 42.1 | 2.5 | 0.8 |
| 1 : 1 | 1.9 | 21.7 | 28.7 | 6.9 | 0.0 |
| 1 : 2 | 6.1 | 15.0 | 22.1 | 1.6 | 1.3 |

## EXPERIMENTAL

For the apparatus, method of operation and analysis of reaction products see [2]. The catalyst was prepared using the directions of V. V. Mazurek [3].

Starting substances: rectified ethyl alcohol (95.5%); the redistilled n-butyric acid had b.p. 161-162°, $d^{20}$ 0.957, $n^{20}D$ 1.3995.

The experiments were all run by the same method, for which reason only one experiment is described (Expt. 6, Table 1). A mixture of ethyl alcohol and n-butyric acid (mole ratio 1 : 1) weighing 43.6 g was passed over the catalyst at 420° and a space velocity of 80. The yield of condensate was 40.1 g (91.9%). The yields of reaction products based on the distillation data and analysis of the fractions were (in % of the condensate): acetone 2.1, methyl propyl ketone 22.8, dipropyl ketone 30.9, and ester 7.5. Analysis of the gas from the experiment (in volume %): $H_2$ 60.0, $CO_2$ 24.7, CO 4.0, $C_nH_{2n}$ 2.5.

The condensates, obtained from the experiments, were fractionally distilled through a rectification column. The following fractions were usually obtained in the distillations: 1st 54-60°, 2nd 60-80°, 3rd 80-100°, 4th 100-150°, 5th 105-125°, 6th 125-140°, 7th 140-145° and residue. The obtained fractions were analyzed for the amount of ketones, aldehydes, acids and esters. Similar fractions from the different experiments were combined for the purpose of redistillation and isolation of pure compounds. The properties of the obtained ketones are given in Table 4.

TABLE 4

Properties of Ketones

| Name of ketone | Boiling point | | $d^{20}_4$ | | $n^{20}_D$ | | Melting point of semicarbazone | |
|---|---|---|---|---|---|---|---|---|
| | found | literature data | found | literature data | found | literature data | found | literature data |
| Acetone ....... | 56.0-57.3° | 56° | 0.7924 | 0.7912 | 1.3593 | 1.3590 | 186.0-186.5° | 188° |
| Methyl propyl ketone ....... | 101.5-102.5 | 102.3 | 0.8077 | 0.8064 | 1.3905 | 1.39012 | 110-111 | 112 |
| Dipropyl ketone .. | 142-143 | 144 | 0.8163 | 0.8175 | 1.4071 | 1.4073 | 131.5-132 | 133 |

Acetone was isolated from the 1st fraction by repeated fractional distillation. The 2nd fraction, representing 4-6% of the total weight of condensates, contained, besides unchanged ethyl alcohol, also butyraldehyde, determined by the method described in [4]. The 3rd fraction was an azeotropic mixture of methyl propyl ketone and water. The 4th fraction was nearly pure methyl propyl ketone. The 5th fraction, representing 3-6% of the total weight of condensates, contained methyl propyl ketone and ethyl butyrate, determined by the usual analysis method. The 6th fraction contained a small amount of dipropyl ketone. The 7th fraction was nearly pure dipropyl ketone. The residues, representing 6-10% of the total weight of condensates, contained up to 40% of dipropyl ketone.

The composition of the gas was characterized by a large content of $H_2$ (60-65%), $CO_2$ (20-25%) and CO (5-10%).

## SUMMARY

1. The passage of a mixture of n-butyric acid and ethyl alcohol over Cr—Mn catalyst gave a 22% yield of methyl propyl ketone based on the weight of starting mixture, and also a 28% yield of dipropyl ketone and a 2% yield of acetone.

2. A scheme was proposed for the formation of mixed ketones from mixtures of acids and primary alcohols.

## LITERATURE CITED

[1] B. N. Dolgov, G. V. Golodnikov and Iu. A. Bol'shukhina, J. Gen. Chem. 27, 2430 (1957).*

[2] B. N. Dolgov and G. V. Golodnikov, J. Gen. Chem. 24, 987 (1954).*

[3] V. V. Mazurek, Dissertation: Catalytic Preparation of Dipropyl Ketone Over Chromium Catalyst [in Russian] (Leningrad State Univ., 1949).

---

*Original Russian pagination. See C.B. translation.

[4] L. N. Petrova and V. D. Zhezmer, Factory Labs., No. 1, 38 (1951).

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# EFFECT OF PRELIMINARY THERMAL DESTRUCTION ON THE OXIDIZABILITY OF METHANE HYDROCARBONS

V. G. Gavrilov and S. A. Velichko

The problem of the oxidation of hydrocarbons has been the subject of a large number of papers, associated both with a study of the phenomenon of knock in internal combustion engines and with the obtaining of various oxygen-containing compounds having independent interest during the oxidation process. In these papers different oxidation mechanisms were proposed [1], the effect of the structure of saturated hydrocarbons on their oxidizability was studied [2], and a quantitative study was made of the oxidizability of various methane hydrocarbons under the same conditions [3]. With the same time of oxidation, temperature, rate of oxygen passage and intensity of irradiation with ultraviolet light the tendency shown by $C_6 - C_9$ hydrocarbons of normal structure to oxidize decreases with increase in the chain length, while all of the iso hydrocarbons, with the exception of isooctane, are more susceptible to oxidation than are their analogs of normal structure [3]. It is known that the octane numbers in the indicated series of normal methane hydrocarbons decrease with increase in the chain length, and that all of the iso hydrocarbons have higher octane numbers than do their analogs of normal structure. The value of the octane number characterizes the resistance to knock, the final reason for which is oxidation.

TABLE 1

| Hydrocarbon | Boiling point | $d^{20}_4$ | $n^{20}D$ |
|---|---|---|---|
| n-Hexane | 68.5° | 0.6609 | 1.3750 |
| 2,3-Dimethylbutane | 58.2° | 0.6622 | 1.3748 |
| n-Heptane | 98.4 | 0.6830 | 1.3874 |
| 2-Methylhexane | 89.7 | 0.6890 | 1.3854 |
| n-Octane | 124.5 | 0.7022 | 1.3970 |
| 2,5-Dimethylhexane | 109.8 | 0.6952 | 1.3930 |
| 2,2,4-Trimethylpentane | 99.8 | 0.6923 | 1.3912 |
| n-Nonane | 149.5 | 0.7166 | 1.4050 |

When the above considerations were compared with the results given in [4], where the relationship between the octane numbers of methane hydrocarbons and the initial temperature of their decomposition was shown, it proved possible to postulate that the oxidation of hydrocarbons is not the primary process in an internal combustion engine. The primary process is the thermal destruction of hydrocarbons, determining further oxidation, which may proceed with normal rates or with unusual rapidity, accompanied by knock.

To verify this postulation was the task of the present study on the preliminary thermal destruction of hydrocarbons and their subsequent oxidation under the same conditions. We took 8 hydrocarbons for study (Table 1).

Partial thermal decomposition of all of the investigated hydrocarbons prior to their oxidation was run in a quartz tube, placed in a furnace at 400°. The given temperature was chosen for the reason that all of the indicated hydrocarbons suffer initial thermal decomposition before 300° [4]. The hydrocarbons were admitted into the tube at a rate of 10 ml per minute. A vaporizer was placed ahead of the tube, and here the temperature was maintained 10° higher than the boiling point of the investigated hydrocarbon. To avoid explosion, a slow stream of nitrogen (constant in all of the experiments) was passed through the tube simultaneously with the hydrocarbon.

After thermal destruction the hydrocarbons were subjected to oxidation, which took place in a quartz vessel through which oxygen was passed at a rate of 10 ml per minute. The time of oxidation was 100 hours, temperature 50°, distance between the vessel and a quartz lamp 20 cm, and amount of hydrocarbon 35 ml.

TABLE 2

| Hydrocarbon | Hydroperoxide oxygen (in %) | Carboxyl oxygen (in %) | Alcohol and water oxygen (in %) | Carbonyl oxygen (in %) | Total amount of oxygen absorbed (in %) |
|---|---|---|---|---|---|
| n-Hexane . . . . . . . . . . . . . . | 0.01 | 0.13 | 0.73 | 0.26 | 1.03 |
| 2,3-Dimethylbutane . . . . . . . . | 1.12 | 1.48 | 5.79 | 5.97 | 14.36 |
| n-Heptane . . . . . . . . . . . . . . | 0.22 | 0.15 | 0.75 | 1.96 | 3.08 |
| 2-Methylhexane . . . . . . . . . . | 0.32 | 0.79 | 2.14 | 2.05 | 5.20 |
| n-Octane . . . . . . . . . . . . . . | 0.35 | 0.23 | 1.22 | 2.15 | 3.95 |
| 2,5-Dimethylhexane . . . . . . . | 1.26 | 1.54 | 5.83 | 6.80 | 15.43 |
| 2,2,4-Trimethylpentane . . . . . | 0.18 | 0.19 | 1.06 | 1.73 | 3.16 |
| n-Nonane . . . . . . . . . . . . . . | 0.44 | 0.35 | 1.30 | 2.20 | 4.29 |

The oxidized hydrocarbons were analyzed for hydroperoxide oxygen by the stannometric method [5], for active hydrogen by the Terent'ev method, for carboxyl oxygen by titration with phenolphthalein as the indicator, and for carbonyl oxygen spectrophotometrically [6]. The amount of alcohol and water oxygen was determined by calculation. The experimental results are given in Table 2.

## SUMMARY

1. The oxidizability of the following hydrocarbons: n-hexane, 2,3-dimethylbutane, n-heptane, 2-methylhexane, n-octane, 2,5-dimethylhexane, 2,2,4-trimethylpentane and n-nonane was investigated after preliminary thermal destruction at 400°.

2. It was shown that the tendency of $C_6 - C_9$ hydrocarbons of normal structure to oxidize is increased by such preliminary thermal treatment, in contrast to a decrease in the oxidizability of the same series of hydrocarbons when not exposed to thermal treatment.

## LITERATURE CITED

[1] H. Callendar, Ind. Eng. Ch. 1927, 123, 147, 182, 210.

[2] S. Krein, Additives to Lubrication Oils [in Russian] (State Scientific and Technical Press of Petroleum and Mineral Oil Literature, 1946).

[3] B. G. Gavrilov and G. Zinov'eva, J. Gen. Chem. 26, 2989 (1956).*

[4] B. G. Gavrilov and L. Bagrat'ian, J. Gen. Chem. 26, 1986 (1956).*

[5] K. Ivanov, Intermediate Products and Intermediate Reactions in the Autooxidation of Hydrocarbons [in Russian] (Gostoptekhizdat, 1949).

[6] G. Lappin, Anal. Chem. 23, 541 (1951).

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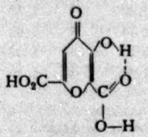
*Original Russian pagination. See C.B. translation.

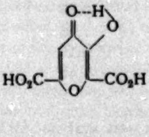
# THE PROBLEM OF THE HYDROGEN BOND IN MECONIC ACID

M. I. Goriaev, V. S. Volkova and G. A. Tolstikov

The structure of meconic acid permits postulating with authority that an intramolecular hydrogen bond is present. The question arises of whether the hydrogen bond in meconic acid is of type (I) or type (II).



(I)



(II)

As is known [1-3], the presence of an intramolecular hydrogen bond in a molecule, containing a hydroxyl and a carboxyl group in the ortho positions, changes the behavior of these groupings substantially. For phenols, containing an intramolecular hydrogen bond, the following are observed: the absence of an abnormal value for the molecular weight when determined in a neutral solvent, a reduction in the acidity, and a difficult formation of esters. Involving the carboxyl group in an intramolecular hydrogen bond leads to an increase in the acidity, an increased difficulty of esterification, and an easier decarboxylation.

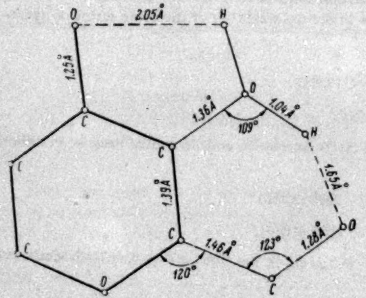


Fig. 1. Diagram of the meconic acid molecule with the interatomic distances taken into account.

Proceeding from the above, we made a study of a number of 3-hydroxy-4-pyrone derivatives. All of the derivatives were obtained from meconic acid, which was isolated from the wastes of the opium industry, the so-called "meconates."

It is possible to elucidate the character of the intramolecular hydrogen bond in meconic acid by comparing the properties of the hydroxyls and carboxyls in meconic and comenic acids, since in the latter it is possible to close the hydrogen bond only in the carbonyl-containing ring.

Determination of the molecular weight of the ethyl esters of comenic and meconic acids, which we ran cryoscopically in naphthalene, revealed that the comenic acid ester shows the greater tendency to associate. It is possible to explain this by different degrees of hydroxyl bonding in these compounds. Apparently, the hydroxyl of meconic acid takes part in the formation of the more stable hydrogen bond. This postulation becomes especially convincing if we turn to the diagram of the meconic acid molecule, constructed in such manner as to retain the interatomic distances and valence angles (Fig. 1). We conditionally took the length of the C—C bonds in the $\gamma$-pyrone ring as equal to 1.39 A, the same as in the case of benzene.

It is known [4] that one of the important factors determining the stability of the hydrogen bond O—H . . . O is the distance H . . . O.

The data shown in the diagram permit giving preference to the theory that the hydrogen bond in meconic acid is of the (I) type, since in this case the interatomic distance O—H . . . O is 0.4 A less than in the case of hydrogen-bond closure according to type (II).

Potentiometric measurement of the dissociation constants of meconic, comenic and pyromeconic acids revealed the pyromeconic acid (3-hydroxy-4-pyrone) when titrated behaves as a typical weak acid. Its dissociation constant has the value $2.2 \cdot 10^{-8}$. It is interesting to mention that as an acid the hydroxypyrone is 100 times stonger than phenol. This fact, reasoning from a similar increase in the strength of pyromucic acid when compared with benzoic acid, may be explained by the influence of the hetero atom [5].

The titration curve of comenic acid has two distinct jumps, corresponding to the dissociation of the carboxyl and the hydroxyl. The dissociation constants have the values: $K_1 = 1.7 \cdot 10^{-2}$, $K_2 = 3.6 \cdot 10^{-8}$. Consequently, the nature of the bonding of the hydroxyl hydrogen in comenic and pyromeconic acids is approximately the same. A slight increase in the acidity of the comenic acid hydroxyl is due to the acceptor action of the carboxyl.

The following dissociation constants were obtained for meconic acid: $K_1 = 6.4 \cdot 10^{-2} - 2.5 \cdot 10^{-1}$, $K_2 = 1.6 \cdot 10^{-2}$, $K_3 = 1.5 \cdot 10^{-10}$. The presence of a hydrogen bond of type (I) in meconic acid led, as was to be expected, to an increase in the acidity of the carboxyl group and to a decrease in the acidity of the hydroxyl group when compared to comenic acid. As an acid the dimeconate ion is 250 times weaker than the monomeconate ion.

When a comparative study was made of the alkylation and benzoylation of the hydroxyls in the diethyl ester of meconic acid and the ethyl ester of comenic acid we found that whereas the hydroxyl of the comenic acid ester is alkylated in quantitative yield by diazomethane, the hydroxyl of the meconic acid ester is nonreactive under these conditions. We were able to obtain the alkyl derivative of the meconic acid ester by reaction of the latter with ethyl iodide in the presence of dry silver oxide.*

Three different methods were used by us to benzoylate the esters of comenic and meconic acid: a) direct reaction with benzoyl chloride, b) by the Schotten-Baumann method, and c) by the Spasov method. The benzoate of the comenic acid ester was obtained by any of the above-mentioned methods in 80-85% yields. We were able to obtain the benzoate of the meconic acid ester by only one of the above-mentioned methods. The difficult alkylation and benzoylation of the meconic acid hydroxyl is due to a reduction in the lability of the hydroxyl hydrogen, which participates in the formation of a stable hydrogen bond of the (I) type.

The fact that meoonic acid can be decarboxylated supports the validity of the postulation that a hydrogen bond of the (I) type is present. Meconic acid suffers decarboxylation when heated above 120°, while comenic acid is decarboxylated when heated at 300°. It should be mentioned that chelidonic acid, devoid of a hydroxyl, is decarboxylated at a temperature exceeding 200° [7].

## EXPERIMENTAL

### Etherification of the Hydroxyl Group

Preparation of the methylate of ethyl comenate. A suspension of 1.84 g of ethyl comenate in 20 ml of dry ether was treated under cooling with an ether solution of diazomethane (2 g-mole). Here the ethyl ester dissolved completely, and the solution after standing for 10-12 hours deposited the ethyl ester of 3-methoxy-4-pyrone-6-carboxylic acid. After two recrystallizations from benzene the obtained compound melted at 156-157°, and failed to give a color with ferric chloride.

Found %: C 55.06, 55.18; H 5.41, 5.32. $C_9H_{10}O_5$. Calculated %: C 54.55; H 5.05.

Preparation of triethyl meconate. A mixture of 2.5 g of diethyl meconate and 4.5 g of ethyl iodide in 25 ml of dry ether, contained in a flask fitted with a reflux condenser, was treated in small portions with 3.45 g of dry powdered silver oxide, and the mixture heated on the water bath until the precipitation of silver iodide ceased.

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* Peratoner obtained the triethylate of meconic acid by reacting ethyl iodide with the trisilver salt [6].

Then the triethyl meconate was extracted from the cooled residue with ether and purified by recrystallization from anhydrous alcohol. M.p. 60-61°.

Benzoylation of ethyl comenate. The direct reaction of benzoyl chloride with ethyl comenate by the G. A. Garkusha method [8] gave the benzoate of ethyl comenate. We were also able to obtain the benzoate in comparable yields by benzoylation using the Schotten-Baumann [9] and Spasov [10] methods.

TABLE 1

| Name of compound | Concentration (in g-mole per 1000 g) | ΔT | M | | Increase in found molecular weight over the calculated (in %) |
|---|---|---|---|---|---|
| | | | found | calculated | |
| Ethyl comenate | 0.16 | 0.97 | 209 | 184 | 13.5 |
| | 0.38 | 2.00 | 241 | | 31.0 |
| Ethyl meconate | 0.12 | 0.80 | 264 | 256 | 3.2 |
| | 0.26 | 1.68 | 268 | | 4.7 |

a) Benzoylation by the Schotten-Baumann method. Three grams of the comenic acid ester was dissolved in 25 ml of 10% potassium hydroxide solution in a wide-mouth flask with ground glass stopper. The obtained solution was treated with stirring in small portions with 2.4 ml of benzoyl chloride. When the odor of benzoyl chloride had disappeared the reaction mixture was poured over ice. The precipitate of the benzoate of ethyl comenate, obtained as needles, was recrystallized from alcohol.

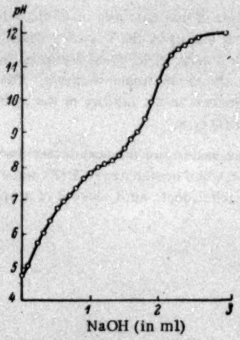

Fig. 2. Curve for the tiration of 25 ml of 0.01 M pyromeconic acid solution with 0.13 N NaOH solution.

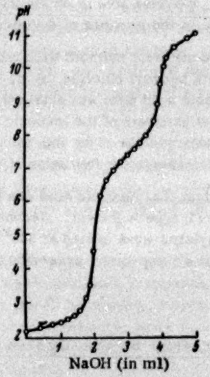

Fig. 3. Curve for the titration of 25 ml of 0.0115 M comenic solution with 0.134 N NaOH solution.

b) Benzoylation by the Spasov method. A solution of 1.84 g of ethyl comenate in 20 ml of benzene was treated with 1.3 ml of benzoyl chloride and 0.15 g of magnesium. The mixture was heated in a glycerin bath at 110-120° for 4 hours. The reaction mixture was treated with saturated soda solution to remove excess unreacted benzoyl chloride and comenic acid ester. The residue was recrystallized from alcohol. The yield of ethyl comenate benzoate was 80% by both benzoylation methods.

The melting point of the benzoates, obtained by the different methods, was 115-116°.

## Cryoscopic Determination of the Molecular Weights of the Ethyl Esters of Meconic and Comenic Acids

A Beckmann apparatus was used to determine the molecular weights. Twice-sublimed naphthalene with m.p. 79.6° was taken as the solvent. The results of the cryoscopic determination of the molecular weights of the ethyl esters of meconic and comenic acids are given in Table 1.

Determination of dissociation constants. For this we used water solutions of carefully purified acids and carbonate-free sodium hydroxide solution. The titrations were run in a nitrogen atmosphere using an LP-5 pH meter and glass electrode.

TABLE 2

$c_{acid} = 0.0115$ M, $c_{alkali} = 0.1340$ N (at 17°)

| NaOH (in ml) | pH | $[C_5H_2O_2(OH)COO^-] \cdot 10^3$ | $[C_5H_2O_2(OH)COOH]$ | $K_1 \cdot 10^2$ |
|---|---|---|---|---|
| 0 | 2.12 | 7.57 | 3.93 | 1.46 |
| 0.2 | 2.17 | 7.81 | 3.59 | 1.47 |
| 0.6 | 2.28 | 8.39 | 2.83 | 1.55 |
| 1.0 | 2.43 | 8.87 | 2.21 | 1.49 |
| 1.4 | 2.58 | 9.74 | 1.13 | 2.27 |
| 1.6 | 2.73 | 9.92 | 0.88 | 2.09 |
| 2.0 | 3.35 | 10.38 | 0.28 | 1.66 |

$K_{average} = 1.7 \cdot 10^{-2}$

a) Pyromeconic acid ($C_5H_3O_2OH$). From the titration curve of an 0.01 M solution (Fig. 2) it can be seen that pyromeconic acid is a very weak acid. Since its pK lies in the range 3-8, then its dissociation constant is easily found from the rule: pK = pH at the half-neutralization point. It has the value $2.2 \cdot 10^{-8}$.

b) Comenic acid [$C_5H_2O_2(OH)COOH$]. The curve for the titration of an 0.0115 M comenic acid solution with sodium hydroxide solution is shown in Fig. 3. The dissociation constant of the carboxyl group exceeds $10^{-3}$, for which reason it was calculated by the method used in the case of phosphoric acid [11]. As the value of the dissociation constant of the carboxyl group in comenic acid we took the average value (Table 2) of the dissociation constant calculated by the equation

$$K_1 = \frac{[H^+][C_5H_2O_2(OH)COO^-]}{[C_5H_2O_2(OH)COOH]}.$$

As is shown in the table, the dissociation constant of the carboxyl group in comenic acid has the value $K_1 = 1.7 \cdot 10^{-2}$. The dissociation constant of the hydroxyl group in comenic acid is easily found using the rule: pH = pK at the half-neutralization point. It is equal to $K_2 = 3.6 \cdot 10^{-8}$.

c) Meconic acid [$C_5HO_2(OH)(COOH)_2$]. Meconic acid when titrated behaves as a strong acid. A sharp jump on the curve (Fig. 4) corresponds to the neutralization of two equivalents of caustic. We calculated the dissociation constant of the second carboxyl group in meconic acid in the same manner as for the case of comenic acid and obtained $K_2 = 1.6 \cdot 10^{-2}$. The absence

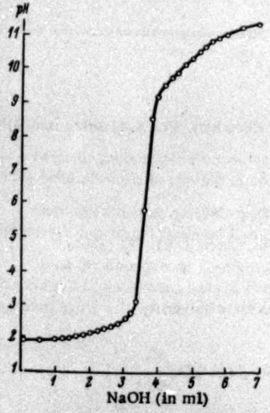

Fig. 4. Curve for the titration of 25 ml of 0.0106 M meconic acid solution with 0.145 N NaOH solution.

of an inflection in the region of neutralizing the first carboxyl grou indicates that in meconic acid $4 < K_1/K_2 < 16$, while the value of the dissociation constant of the first carboxyl should lie in the range $6.4 \cdot 10^{-2} - 2.5 \cdot 10^{-3}$. To determine the dissociation constant of the hydroxyl group in meconic acid we titrated a 0.1 M solution of disodium meconate with 0.4380 N NaOH solution. The dissociation constant was calculated using the equation [12]

$$pK = pH + \lg I^{--} - \lg I^{---},$$

where $I^{--}$ is the amount of the diion $C_6HO_2(OH)(COO^-)_2$ (in g-mole), $I^{---}$ is the amount of the triion $C_6HO_2(O^-)(COO^-)_2$ (in g-mole), and $I^{--} + I^{---}$ is the total amount of disodium meconate. In view of the fact that the triion tends to hydrolyze, it is necessary to make a correction for the concentration of OH ions in the solution.

$$I^{---} = v_{OH} \cdot H \cdot 10^{-3} - v \cdot 10^{pH-14} \cdot 10^{-3},$$

where $v_{OH} \cdot H \cdot 10^{-3}$ is the number of g-equiv of added caustic, and $\underline{v}$ is the total volume of the solution.

The third dissociation constant of meconic acid has the value $K_3 = 1.5 \cdot 10^{-10}$.

## SUMMARY

1. It was shown that a stable intramolecular hydrogen bond, closed into a six-membered ring, is present in meconic acid.

2. The dissociation constants of meconic, comenic and pyromeconic acids were determined by potentiometric titration.

3. The previously unknown ethyl ester of 3-methoxy-4-pyrone-6-carboxylic acid was synthesized.

## LITERATURE CITED

[1] L. E. Lutskii, Advances in Chemistry [in Russian] 23, 479 (1954).

[2] M. I. Batuev, Advances in Chemistry 10, 416 (1941).

[3] Arnold, Sprung, J. Am. Chem. Soc. 61, 2475 (1939).

[4] N. D. Sokolov, Advances in Physical Sciences [in Russian] 2, 205 (1955).

[5] Ostwald, Z. phys. Ch. 3, 339.

[6] A. C. Peratoner, Zbl. 8, 407 (1897).

[7] R. Willstätter and R. Pummerer, Ber. 37, 3777 (1904).

[8] G. A. Garkusha, J. Gen. Chem. 16, 2025 (1946).

[9] J. F. Thorpe and M. A. Whitely, Thorpe's Dictionary of Applied Chemistry, Vol. 2, [Russian translation], pp. 155-157 (1937).

[10] A. Spasov, Ber. 75B-2, 779 (1942).

[11] H. T. S. Britton, Hydrogen Ions [Russian translation] (ONTI, 1936), p. 160.

[12] E. A. Shilov, I. V. Smirnov-Zamkov and K. I. Matkovskii, Ukrain. Chem. J. 21, 611 (1955).

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# ORGANIC SULFUR COMPOUNDS

## III. PROPERTIES OF HALOALKENE-, ALKENE- AND HALOALKENESULFONYL FLUORIDES

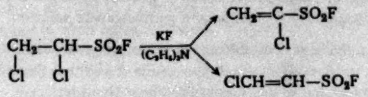
B. M. Gladshtein, V. N. Chernetskii, M. I. Kiseleva and L. Z. Soborovskii

As had been found earlier [1], potassium fluoride is not only a fluorination agent, but it also functions as an agent for the dehydrohalogenation of the halo derivatives of alkanesulfonyl chlorides, converting them into unsaturated sulfonyl fluorides.

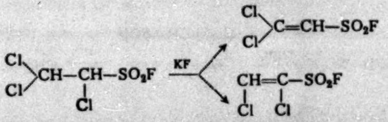
In the present study it was established that the halo derivatives of alkanesulfonyl fluorides are also capable of undergoing similar transformations.

Thus, β,β-dichloroethanesulfonyl fluoride, described in a previous communication [2], is dehydrochlorinated by potassium fluoride to β-chlorovinylsulfonyl fluoride.

The α,β-dichloro- and α,β,β-trichloroethanesulfonyl fluorides are also capable of similar transformations.



(1)

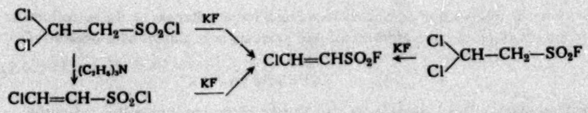


(2)

As starting substances for running these reactions we used the vinyl- and β-chlorovinylsulfonyl fluorides, the double bond of which is capable of adding chlorine in the normal manner.

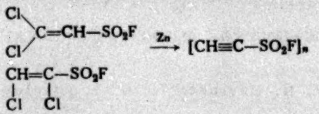
From the schemes given above it is obvous that the dehydrochlorination of the α,β-dichloro- and α,β,β-trichloroethanesulfonyl fluorides should lead to a mixture of isomeric mono- and dichloroethenesulfonyl fluorides.

Since the constants of β-chlorovinylsulfonyl fluoride synthesized by us by several routes were known, then the isolation of the second isomer, namely α-chlorovinylsulfonyl fluoride, should not have presented any difficulties [Scheme (1)].



However, it proved that the instability of α-chlorovinylsulfonyl prevents its isolation under the conditions of reaction with potassium fluoride, as a result of which it was obtained by the action of triethylamine on α, β-dichloroethanesulfonyl fluoride with cooling to −50°.

The mixture of isomers obtained in the dehydrochlorination of α,β,β-trichloroethanesulfonyl fluoride could not be separated by conventional fractional distillation. To separate the obtained mixture we employed reaction with zinc dust. The action of zinc on a mixture of α,β- and β,β-dichlorovinylsulfonyl fluorides leads to the situation that in the first 20 minutes a sample of the reactant mixture gives a positive test for α-acetylenic hydrogen, but because of ensuing polymerization and tarring it becomes impossible to subsequently show its presence.



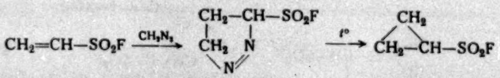
However, this method also did not permit us to isolate one of the components of the isomeric mixture, since fractional distillation of the reaction products gave us only some of the unreacted starting mixture.

In addition to the above-mentioned chlorination some of the reactions of the double bond found in the α-position to the sulfofluoride group were studied in the present paper (reaction with bromine, hydrogen fluoride, potassium permanganate and diazomethane).

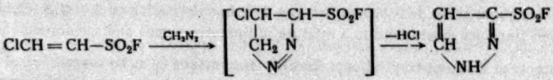
It was found that vinylsulfonyl fluoride, vinylsulfonyl chloride, α-chlorovinylsulfonyl fluoride, β-chlorovinylsulfonyl chloride and β-chlorovinylsulfonyl fluoride readily add chlorine at the double bond with the formation of the corresponding di- and trichlorides, and that they do not decolorize bromine in carbon tetrachloride solution.

Vinylsulfonyl fluoride does not add either liquid or gaseous hydrogen fluoride. All of the above mentioned unsaturated compounds decolorize acidified potassium permanganate solution.

The addition of diazomethane to vinylsulfonyl fluoride proceeds smoothly at the double bond without involving the acid fluoride ion, as a result of which pyrazoline-3-sulfonyl fluoride is formed, capable of losing nitrogen when heated with conversion to cyclopropanesulfonyl fluoride:



β-Chlorovinylsulfonyl fluoride behaves differently in this reaction, and, adding diazomethane, is converted into a stable pyrazole system (as the result of spontaneous dehydrochlorination), which fails to decompose when heated.



The course of this reaction is apparently similar to the described dehydrochlorination of a chloro-substituted ketone of the pyrazoline series, where a pyrazole ring is formed [3].

From the above it follows that an unsaturated bond, found adjacent to the sulfofluoride group, is similar in its properties to the unsaturated bond of vinylsulfonic acid, its salts and its halo derivatives.

## EXPERIMENTAL

α,β-Dichloroethanesulfonyl fluoride (I). A solution of 12 g of vinylsulfonyl fluoride in 100 ml of carbon tetrachloride was chlorinated with chlorine gas for 8 hours with illumination by a 200-watt lamp. We obtained 13.5 g of (I) (yield 68.5%).

B.p. 162-163° (752 mm), $n^{20}D$ 1.4460, $d^{20}_4$ 1.6637, $MR_D$ 29.06; calc. 29.68.

Found %: C 14.01, 13.22; H 1.57, 1.74; S 17.99, 18.29; F 12.2, 12.9. $C_2H_3O_2SFCl_2$. Calculated %: C 13.29; H 1.66; S 17.71; F 10.5.

α,β-Dichloroethanesulfonyl chloride (II). A solution of 4.0 g of vinylsulfonyl chloride* in 40 ml of carbon tetrachloride was chlorinated for 8 hours with illumination. Fractional distillation gave 3 g of (II).

B.p. 100-103° (10 mm), $n^{20}D$ 1.5019, $d^{20}_4$ 1.6509, $MR_D$ 35.28; calc. 35.01.

Found %: S 15.68, 15.43. $C_2H_3O_2SCl_2$. Calculated %: S 16.2.

α,α,β-Trichloroethanesulfonyl fluoride (III). The chlorination of a solution of 4.5 g of α-chlorovinylsulfonyl fluoride [112-115° (749 mm), $n^{20}D$ 1.4140] in 50 ml of carbon tetrachloride under the above-described conditions gave (III).

B.p. 165-167° (749 mm), $n^{20}D$ 1.4580, $d^{20}_4$ 1.7149, $MR_D$ 34.29; calc. 34.63.

Found %: F 8.8, 8.6. $C_2H_2O_2SFCl_3$. Calculated %: F 8.8.

α,β,β-Trichloroethanesulfonyl fluoride (IV) was obtained by the chlorination of 57.6 g of β-chlorovinylsulfonyl fluoride [b.p. 43-45° (25 mm), $n^{20}D$ 1.4358] in 250 ml of carbon tetrachloride. The fraction corresponding to (IV) was collected (74.6 g).

B.p. 84-86° (25 mm), b.p. 48-49° (2 mm), $n^{20}D$ 1.4658, $d^{20}_4$ 1.7303, $MR_D$ 34.50; calc. 34.63.

Found %: F 8.5, 8.7. $C_2H_2O_2SFCl_3$. Calculated %: F 8.8.

α-Chlorovinylsulfonyl fluoride (V). A solution of 13 g of dry triethylamine in 22 ml of absolute ether was added in drops with stirring and cooling to −50° to a solution of 13.5 g of (I) in 55 ml of absolute ether. The mixture was stirred with cooling for 2.5 hours, then brought to room temperature, and treated with 100 ml of 1% sulfuric acid cooled to 0°. The ether layer was separated and washed first with 1% sulfuric acid, then with 20% sodium chloride solution, next with water, and finally it was dried over sodium sulfate. The following fractions were collected on fractional distillation: 1st, 18-21°, (5 mm), $n^{20}D$ 1.4080, $d^{20}_4$ 1.4710, 4 g; 2nd 21-23° (5 mm), $n^{20}D$ 1.4190, $d^{20}_4$ 1.5158, 2.1 g. Redistillation of the 1st fraction gave pure (V).

B.p. 116-117° (779 mm), $n^{20}D$ 1.4070, $d^{20}_4$ 1.4673, $MR_D$ 24.25; calc. 24.44.

Found %: C 17.55, 17.85; H 1.71, 1.96; S 22.72, 22.52; F 14.14, 14.57. $C_2H_2O_2SFCl$. Calculated %: C 16.61; H 1.39; S 22.19; F 13.5.

In contrast to β-chlorovinylsulfonyl fluoride, (V) is unstable and oxidizes rapidly when stored. The 2nd fraction is apparently β-chlorovinylsulfonyl fluoride with (V) as impurity.

Action of potassium fluoride on (I).

The effect of potassium fluoride on (I). (I) is treated with a saturated water solution of potassium fluoride under the conditions described previously [11]. The organic layer is dried by calcium chloride and then it is distilled, yielding 8 g of a substance with boiling point of 130-134° (760 mm), $n_D^{20}$ 1.4162, $d_4^{20}$ 1.5379. This substance is identical to the β-chlorovinylsulfonyl fluoride which was synthesized earlier.

The effect of potassium fluoride on (IV). As indicated in the present paper, 21.5 g of (IV) was reacted with a 6-fold excess of saturated aqueous potassium fluoride solution. The fraction with b.p. 52-54° (25 mm) was collected.

$n_D^{20}$ 1.4538, $d_4^{20}$ 1.6222, $MR_D$ 29.90.

Found %: S 17.09, 17.19; Cl 39.47, 39.37; F 10.0, 10.6. $C_2HO_2SFCl$. Calculated %: S 17.90; Cl 39.59; F 10.06.

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*Vinylsulfonyl chloride was isolated in the preparation of β-chloroethanesulfonyl chloride as the fraction with b.p. 158-160° (754 mm), b.p. 60-68° (20 mm), $n^{20}D$ 1.4700, $d^{20}_4$ 1.4098, $MR_D$ 25.05 [2].

The obtained substance is apparently a mixture of the isomeric α,β- and β,β-dichlorovinylsulfonyl fluorides, which could be formed in the cleavage of one molecule of hydrogen chloride from (IV). However, taking into consideration the specific properties of one of the possible isomers, mentioned in the preceding experiment, it is possible to postulate that the β,β-dichlorovinylsulfonyl fluoride predominates in the indicated mixture.

Twelve grams of the obtained mixture of unsaturated dichlorosulfonyl fluorides was treated in the cold with an equimolar amount of zinc dust in anhydrous alcohol. After filtration and removal of the solvent in vacuo the residue represented a tarry substance that could not be distilled.

In a second experiment 28.9 g of mixed α,β- and β,β-dichlorovinylsulfonyl fluorides was mixed with 30 g of zinc dust in 100 ml of absolute ether. Samples were removed from the reaction mixture at periodic intervals and tested with Ilosvay reagent. The first samples (after 5, 10, 15 and 20 minutes) gave a distinct positive test with the reagent. Then the Ilosvay reaction became negative. The reaction with zinc dust was run for 5 hours, after which the solids were removed by filtration, the ether evaporated, and the residue fractionally distilled. The fraction with b.p. 52-54° (25 mm), corresponding to the original substance, was collected (18.5 g); the residue was a hard tarry substance.

Action of diazomethane on vinylsulfonyl fluoride. An ether solution of diazomethane was added with stirring and cooling to − 10° to a solution of 17 g of vinylsulfonyl fluoride in 75 ml of ether. Then the mixture was stirred at room temperature for 1 hour and allowed to stand overnight. The next day the ether was distilled off; the residue crystallized as bright yellow tablets, melting at 30°. The obtained pyrazoline-3-sulfonyl fluoride (VI) is unstable and suffers partial decomposition even at room temperature. It begins to decompose violently at 125° with the evolution of nitrogen.

Found %: N 17.5, 17.2. $C_3H_5O_2NSF$. Calculated %: N 18.4.

(VI) is completely soluble in hydrochloric acid, forming the hydrochloride, which was isolated as yellow crystals.

Pyrolysis of (VI). (VI) was placed in a flask and heated cautiously to 125° to decompose it, collecting the liquid distillate. The obtained distillate was refluxed for 20 minutes and then distilled again, collecting the fraction with b.p. 153-154.5° (750 mm).

$n^{20}D$ 1.4220, $d^{20}_4$ 1.3426, $MR_D$ 23.50, $EM_D$ 0.34.

Found %: F 15.03, 14.72. $C_3H_5O_2SF$. Calculated %: F 15.3.

On the basis of the constants, analysis and the presence of molecular-refraction exaltation it is possible to assign the structure of cyclopropanesulfonyl fluoride to the obtained substance.

Action of diazomethane on β-chlorovinylsulfonyl fluoride (VII). A solution of 12 g of (VII) in 30 ml of absolute ether was cooled to − 40°, and then an ether solution of diazomethane was added with stirring until the color of the diazomethane ceased to disappear, after which the mixture was warmed up to room temperature. After removal of the solvent and original (VII) by distillation the residue solidified as yellow crystals with m.p. 125-126° (from benzene).

Found %: S 21.86, 21.59; N 18.29, 18.03. $C_3H_3O_2N_2SF$. Calculated %: S 21.2; N 18.65.

## SUMMARY

1. Seven new sulfonyl fluorides were synthesized: α, β-dichloroethane-, α,α,β- and α,β, β-trichloroethane-, α-chlorovinyl-, cyclopropane-, pyrazoline-3- and pyrazole-3-sulfonyl fluorides.

2. α,β-Dichloroethanesulfonyl chloride, and also α,β- and β,β-dichlorovinylsulfonyl fluorides (as a mixture of isomers), were synthesized.

3. The dehydrohalogenating action of potassium fluoride on α,β-dichloroethanesulfonyl fluoride leads mainly to the formation of β-chlorovinylsulfonyl fluoride.

## LITERATURE CITED

[1] L. Z. Soborovskii, B. M. Gladshtein, V. N. Chernetskii and M. I. Kiseleva, J. Gen. Chem. 28, 1866 (1958).*

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*Original Russian pagination. See C.B. translation.

[2] L. Z. Soborovskii, B. M. Gladshtein, M. I. Kiseleva and V. N. Chernetskii, J. Gen. Chem. 28, 1870 (1958).*

[3] A. N. Nesmeianov and I. K. Kochetkov, Proc. Acad. Sci. USSR 78, 65 (1951).

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*Original Russian pagination. See C.B. translation.

# PREPARATION OF ORGANOSILICON HYDROXY COMPOUNDS FROM AMINOSILANES

## I. PREPARATION OF ALKYLALKOXYSILANES FROM ALKYLPHENYLAMINOSILANES SYNTHESIZED FROM ALKYLCHLOROSILANES

A. P. Kreshkov, L. V. Myshliaeva and L. M. Khananashvili

The range of practical application of organosilicon compounds expands in measure with the development of their chemistry. The alkylalkoxysilanes [1] find great practical utility in the modification of various classes of inorganic and organic compounds and as intermediates in the synthesis of high-molecular organosilicon compounds. The following methods for the preparation of alkylalkoxysilanes are described in the literature.

1) Alkylation of alkoxysilanes or haloalkoxysilanes using organozinc compounds and metallic sodium [2]

$$2(RO)_3SiCl + ZnR'_2 + 2Na \rightarrow 2R'Si(OR)_3 + Zn + 2NaCl$$

or

$$2Si(OR)_4 + ZnR'_2 + 2Na \rightarrow 2R'Si(OR)_3 + Zn + 2RONa$$

2) Alkylation of alkoxysilanes or haloalkoxysilanes using either organomagnesium [3-5] or organolithium compounds [6, 7]

$$Si(OR)_4 + R'MgX \rightarrow R'Si(OR)_3 + MgXOR$$

or

$$(RO)_3SiCl + R'MgX \rightarrow R'Si(OR)_3 + MgXCl$$

3) Replacement of hydrogen in alkylsilanes by alkoxy groups using alcohols in the presence of alcoholates of lithium, sodium, potassium and rubidium [8]

$$R'O^- + R_3SiH \rightarrow [R'O\ldots R_3Si\ldots H]^- \xrightarrow{+R'OH} R'OSiR_3 + H_2 + R'O^-$$

4) Esterification of alkylhalosilanes using alcohols

$$R'_xSiCl_{4-x} + (4-x)\,ROH \rightarrow R'_xSi(OR)_{4-x} + (4-x)HCl$$

However, the existing methods of synthesizing alkylalkoxysilanes suffer from a large number of disadvantages. The first method, proposed more than 80 years ago, is not used at the present time even in the laboratory due to the complexity of the synthesis conditions (operating with sealed tubes, possibility of explosions, etc.). The second method is characterized by being quite long (8-12 hours and more is required for the synthesis), and is associated with great experimental difficulties and the use of highly inflammable solvents. With this method it is quite difficult to obtain a product of definite composition, and usually a mixture of alkylalkoxysilanes is obtained. This method is also not feasible economically. The third method, recently proposed by Dolgov and co-workers [8], possesses interest. In this case reaction is more rapid (4-5 hours), and the yields are substantially higher. The indicated methods possess essentially, preparative significance, and not industrial importance.

Only the fourth method is economically feasible. However in this case the main reaction is accompanied by side reactions, leading to a substantial reduction in the yields of alkylalkoxysilanes. In addition, the synthesis requires a large amount of time.

We developed a new method for the preparation of alkylalkoxysilanes, based on the exchange reaction of alkylchlorosilanes with aniline (a) and subsequent reaction of the resulting alkylphenylaminosilanes with alcohols (b)

$$R_xSiCl_{4-x} + 2(4-x)C_6H_5NH_2 \rightarrow R_xSi(NHC_6H_5)_{4-x} + (4-x)C_6H_5NH_2 \cdot HCl, \qquad (a)$$

$$R_xSi(NHC_6H_5)_{4-x} + (4-x)R'OH \rightarrow R_xSi(OR')_{4-x} + (4-x)C_6H_5NH_2. \qquad (b)$$

Reaction "a" goes in quantitative yields for aniline and a whole series of amines [9]. As our investigations revealed, reaction "b" goes in very high yields (80-95%).

We used the proposed method to synthesize trimethylmethoxysilane, dimethyldimethoxysilane, trimethylethoxysilane and dimethyldiethoxysilane.

## EXPERIMENTAL

Synthesis of trimethylmethoxysilane (I). Into a round-bottomed flask was charged 108.5 g of trimethylchlorosilane and 204-6 g of freshly distilled aniline, previously dried over fused sodium hydroxide. The reaction was accompanied by substantial heat-evolution. The flask was closed with a stopper fitted with a reflux condenser and the flask contents were stirred for 10-15 minutes, after which the obtained alkylphenylaminosilane was treated with 35.2 g of anhydrous methyl alcohol and the mixture stirred for 10-15 minutes. Then the flask with contents was heated on the boiling water bath for 15-20 minutes. After this the reaction product was distilled through a fractionating column and the fraction with b.p. 57-58° collected. The yield of (I) was 95.6 g (91%).

$d^{20}_4$ 0.758, $n^{20}D$ 1.3680.

Found %: C 45.18; H 11.55; Si 26.85. $C_4H_{12}OSi$. Calculated %: C 46.15; H 11.54; Si 26.92.

It is possible to sublime small amounts of aniline hydrochloride if the heating is nonuniform during the distillation of (I). In such case the aniline hydrochloride is easily separated from (I) by either suction-filtration or filtration.

The other alkylalkoxysilanes were synthesized in a similar manner.

Synthesis of dimethyldimethoxysilane (II). For the synthesis we took 129 g of dimethyldichlorosilane, 409.2 g of aniline and 70.4 g of anhydrous methyl alcohol. The (II) fraction boiling in the range 81-83° was collected. Yield 106 g (87%).

$d^{20}_4$ 0.849, $n^{20}D$ 1.3669.

Found %: C 39.56; H 10.21; Si 23.24. $C_4H_{12}O_2Si$. Calculated %: C 39.99; H 10.00; Si 23.33.

Synthesis of trimethylethoxysilane (III). For reaction we took 108.5 g of trimethylchlorosilane, 204.6 g of aniline and 50.6 g of anhydrous alcohol. The (III) fraction boiling in the range 75-76° was collected. Yield 110 g (93%).

$d^{20}_4$ 0.757, $n^{20}D$ 1.3745.

Found %: C 50.23; H 11.07; Si 25.03. $C_5H_{14}OSi$. Calculated %: C 50.74; H 11.83; Si 23.67.

Synthesis of dimethyldiethoxysilane (IV). For reaction we took 129 g of dimethyldichlorosilane, 409.2 g of aniline and 101.2 g of anhydrous alcohol. The fraction boiling in the range 112-115° was collected. Yield 112 g (80%).

$d^{20}_4$ 0.884, $n^{20}D$ 1.3855.

Found %: C 49.09; H 10.65; Si 18.92. $C_6H_{16}O_2Si$. Calculated %: C 48.59; H 10.78; Si 18.88.

In case of necessity, the aniline hydrochloride formed during reaction can be recovered by treating with alkaline agents, and reused in the preparation of alkylalkoxysilanes.

Silicon was determined gravimetrically as $SiO_2$ [10]. The amount of carbon and hydrogen was determined by the Pregl method of combustion [11] using $Cr_2O_3$ as the catalyst [12].

All of the synthesized products were characterized by a high purity and did not require supplemental purification.

## SUMMARY

A new method was developed for the synthesis of alkylalkoxysilanes based on the reaction of alkylchlorosilanes with aniline and subsequent treatment of the obtained alkylphenylaminosilanes with alcohols. The yields of the products ranged from 80 to 95%.

## LITERATURE CITED

[1] A. P. Kreshkov, Organosilicon Compounds in Industry [in Russian] (Industrial Construction Literature Press, 1956), 2nd ed.

[2] C. Friedel and J. Crafts, Ann. Chim. Phys. 9, 5 (1866).

[3] E. Khotinsky and B. Seregenkoff, Ber. 41, 2946 (1908).

[4] M. N. Kalinin, Proc. Acad. Sci. USSR 26, 373 (1940).

[5] H. W. Post, The Chemistry of Aliphatic Orthoesters, N.Y. (1943).

[6] H. Gilman and R. Clark, J. Am. Chem. Soc. 69, 1499, (1947).

[7] A. D. Petrov and T. I. Chernysheva, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1955, 820.*

[8] B. N. Dolgov, P. N. Kharitonov and M. G. Voronkov, J. Gen. Chem. 24, 1178 (1954).*

[9] E. Larsson and L. Bjellerup, J. Am. Chem. Soc. 75, 995 (1953).

[10] L. M. Khananashvili, Dissertation: Reaction of Tetraalkoxy- and Alkylalkoxysilanes and Their Derivatives with Some Inorganic Compounds [in Russian] (D. I. Mendeleev Moscow Institute of Chemical Technology, 1957).

[11] K. Weigand, Experimental Methods in Organic Chemistry [Russian translation] (IL, 1951), Vol. 3.

[12] V. A. Klimova, M. O. Korshun and E. G. Bereznitskaia, Proc. Acad. Sci. USSR 96, 81 (1954).

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# HYDROLYSIS OF AROMATIC SULFONIC ACID ESTERS

## VI. ALKALINE AND AQUEOUS HYDROLYSIS OF NITRO-SUBSTITUTED ARYL SULFONATES

R. V. Vizgert and E. K. Savchuk

In previous communications, devoted to a study of the hydrolysis kinetics of aryl sulfonates [1, 2], it was shown that the presence of electronegative substituents in the benzenesulfonic acid, as well as in the phenol [3], accelerates the hydrolysis rate of aryl sulfonates when compared to the unsubstituted esters. Of all of the electronegative substitutents the nitro group exerts the greatest accelerating effect; the effect of the position of the nitro group on the hydrolysis rate of nitro-substituted aryl sulfonates is different and depends on whether the nitro group is found in the benzenesulfonic acid or in the phenol. Nitro groups in the ortho position reduce the hydrolysis rate, if found in the benzenesulfonic acid, and increase it, if found in the phenol.

It seemed of interest to follow the manner in which increasing the number of nitro groups in the phenol and in the benzenesulfonic acid would affect the alkaline hydrolysis rate, and also to determine if nitro-substituted aryl sulfonates could be hydrolyzed by water, all the more so since it is known from the literature that phenyl benzenesulfonate is not hydrolyzed by water [2, 4].

## EXPERIMENTAL

The esters subjected to alkaline hydrolysis were the esters of 2,4-dinitrophenol with benzenesulfonic acid (1), 2-nitrobenzenesulfonic acid (2) and 4-chlorobenzenesulfonic acid (3) (the last ester was graciously supplied by O. N. Prib), the esters of 2,4-dinitrobenzenesulfonic acid with phenol (4) and 2-nitrophenol (5), and the ester of 3,5-dinitrobenzenesulfonic acid with phenol (6). The above indicated esters, and also the mononitro-substituted aryl sulfonates containing the nitro group both in the phenol and in the benzenesulfonic acid, were also subjected to aqueous hydrolysis in the absence of caustic.

TABLE 1

| Expt. No. | Formula | Melting point | Sulfur content (%) | |
|---|---|---|---|---|
| | | | found | calc. |
| 1 | $C_6H_5SO_2OC_6H_3(NO_2)_2$-2,4 . . . . | 118—119° | 9.93 | 9.88 |
| 2 | 2-$NO_2C_6H_4SO_2OC_6H_3(NO_2)_2$-2,4 | 121 | 8.78 | 8.67 |
| 3 | 4-Cl-$C_6H_4SO_2OC_6H_3(NO_2)_2$-2,4 | 116—118 | | |
| 4 | 2,4-$(NO_2)_2C_6H_3SO_2OC_6H_5$ . . . . | 115—116 | 9.91 | 9.88 |
| 5 | 2,4-$(NO_2)_2C_6H_3SO_2OC_6H_4NO_2$-2 | 139 | 8.71 | 8.67 |
| 6 | 3,5-$(NO_2)_2C_6H_3SO_2OC_6H_5$ . . . . | 101 | 9.96 | 9.88 |

Only the esters of mononitrobenzenesulfonic acid are described in the literature [5]; with the exception of (4) and (5), the esters of dinitrobenzenesulfonic acid are unknown [6]. To obtain them we used the general method for the synthesis of aryl sulfonates [7], with some modification of the experimental technique. To a solution of 4.3 g of o-nitrobenzenesulfonyl chloride in 50 ml of anhydrous alcohol was added at room temperature, with mechanical stirring, in small portions, 4 g of sodium 2,4-dinitrophenolate in 2 hours. Then the stirring was continued for another 2 hours. The obtained precipitate of ester and NaCl was filtered and washed with water. The ester is very difficultly soluble in alcohol and remains almost entirely on the filter. Removal of 30 ml of alcohol from the mother liquor by distillation yielded an additional small amount of the ester. The yield of crude product was 6.2 g, which after two recrystallizations from alcohol gave 5.5 g of the ester (77%), m.p. 121-122°.

All of the other esters were obtained in a similar manner in good yield. The reactants — sulfonyl chloride and phenolate — were taken in a 1 : 1 ratio. The esters of the nitro- and dinitrobenzenesulfonic acids, together with their melting points and analysis, are given in Table 1.

The method used by us to study the hydrolysis rate is described in a previous communication [8]. The method of Hess and Frahm [9] was used to purify the dioxane. The purity of the esters was verified by melting point, analysis for sulfur, and final titration result. The saponification was run in 70% water-dioxane medium with caustic at 0 and at 15°. The hydrolysis rate of esters (1), (2), (3) and (5) was determined by back-titration of the excess acid with caustic in the presence of methyl red as the indicator, while esters (4) and (6) were titrated in the presence of rosolic acid as the indicator.

TABLE 2

| 0° | | | | 15° | | | |
|---|---|---|---|---|---|---|---|
| t (min) | $a - x$ | $b - x$ | $k$ | t (min) | $a - 2x$ | $b - x$ | $k$ |
| 0 | 0.00830 | 0.00312 | — | 0 | 0.00830 | 0.00312 | — |
| 3.5 | 0.00593 | 0.00193 | 0.334 | 3 | 0.00459 | 0.00125 | 0.870 |
| 6 | 0.00498 | 0.00144 | 0.341 | 6 | 0.00346 | 0.00067 | 0.880 |
| 12 | 0.00393 | 0.00090 | 0.357 | 8 | 0.00308 | 0.00048 | 0.880 |
| 16 | 0.00336 | 0.00061 | 0.334 | 14 | 0.00251 | 0.00019 | 0.890 |
| | | $k_{mean}$ = | 0.341 | | | $k_{mean}$ = | 0.880 |

TABLE 3

| t (min) | $a - 2x$ | $b - x$ | $k$ |
|---|---|---|---|
| 0 | 0.00803 | 0.00282 | — |
| 3 | 0.00471 | 0.00133 | 1.406 |
| 5 | 0.00413 | 0.00107 | 1.180 |
| 9 | 0.00336 | 0.00072 | 1.040 |
| 14 | 0.00258 | 0.00037 | 1.233 |
| | | $k_{mean}$ = | 1.215 |

The saponification was run in a 100-ml flask with a side tube; the weighed substance was added through the side opening, while the alkaline water-dioxane solution was introduced through the expanded portion of the flask, after which the flask was shaken vigorously and then samples removed at definite time intervals. Reaction was terminated by pouring the samples (20 ml) into 0.05 N HCl solution cooled to 0°. The initial concentration of the ester was 0.0031 g-mole/liter, and that of the KOH was 0.0084 g-mole/liter. The hydrolysis rate constants were calculated using the 2nd order equation, with allowance made for the double consumption of alkali: $dx/dt = k(a - 2x)(b - x)$, where $\underline{a}$ is the alkali concentration, and $\underline{b}$ is the ester concentration.

The energy of activation was calculated using the equation

$$E = \frac{(\log k_2 - \log k_1) \cdot 4.575 T_1 T_2}{T_2 - T_1},$$

and the pre-exponential coefficient using the equation: $k = P_z \cdot e^{-E/RT}$. The data of several typical experiments on the hydrolysis of the esters of 2,4-dinitrophenol with benzenesulfonic acid and 2-nitrobenzenesulfonic acid are given in Tables 2 and 3, while the summary data on the hydrolysis of the nitro-substituted aryl sulfonates are given in Table 4. The dimensions of the terms are: k – liter/g-mole · sec, E – cal/g-mole, log $P_z$ – liter/g-mole · sec.

To study aqueous hydrolysis the weighed amount of ester (0.0015 g-mole) was dissolved in 20 ml of 70% water-dioxane solution and then heated for a long time (Table 5) in flasks fitted with reflux condensers. The acid formed as the result of hydrolysis was titrated with 0.0368 N KOH in the presence of the earlier indicated indicators. The percent of hydrolyzed ester was determined from the amount of alkali consumed.

TABLE 4

| Expt. No. | Formula | $k_0 \cdot 10^3$ | $k_{18} \cdot 10^3$ | $E$ | log $P_z$ |
|---|---|---|---|---|---|
| 1 | $C_6H_5SO_2OC_6H_3(NO_2)_2$-2,4 | 339.0 | 880.0 | 9350 | 7.02 |
| 2 | 2,4-$(NO_2)_2C_6H_3SO_2OC_6H_5$ | 38.0 | 183.0 | 16360 | 11.68 |
| 3 | 3,5-$(NO_2)_2C_6H_3SO_2OC_6H_5$ | 1.45 | 5.8 | 14390 | 8.67 |
| 4 | 2-$NO_2C_6H$ $SO_2OC_6H_3(NO_2)_2$-2,4 | 2450.0 | — | — | — |
| 5 | 2,4-$(NO_2)_2C_6H_3SO_2OC_6H_4NO_2$-2 | 2150.0 | — | — | — |
| 6 | 2-$ClC_6H_4SO_2OC_6H_3(NO_2)_2$-2,4 | 1250.0 | — | — | — |

Parallel experiments were also run on studying the hydrolysis rate at 120°. For this 0.00015 g-mole of the ester was dissolved in 20 ml of 70% dioxane-water solution and then sealed in ampuls. On conclusion of reaction the ampuls were opened, the solution poured out, the ampuls rinsed with 10 ml of water-dioxane solution, and the sample titrated as indicated above.

TABLE 5

| Formula | Heating at 80° | | | Heating at 120° | | |
|---|---|---|---|---|---|---|
| | time (hrs) | number of ml of KOH | percent reacted ester | time (hrs) | number of ml of KOH | percent reacted ester |
| $C_6H_5SO_2OC_6H_4NO_2$-2 | 92 | 0.95 | 21.2 | — | — | — |
| $C_6H_5SO_2OC_6H_3(NO_2)_2$-2,4 | 44.5 | 3.9 | 46 | 37.5 | 5.1 | 60.3 |
| 2,4-$(NO_2)_2C_6H_3SO_2OC_6H_5$ | 44.5 | 0.2 | 4 | 37.5 | 0.3 | 5 |
| 2-$NO_2C_6H$ $SO_2OC_6H_3(NO_2)_2$-2,4 | 45.5 | 6.6 | 82.7 | 40.0 | 8.46 | 100 |
| 2,4-$(NO_2)_2C_6H_3SO_2OC_6H_4NO_2$-2 | 45.5 | 0.5 | 6 | 40.0 | 0.7 | 7.5 |
| 4-$ClC_6H_4SO_2OC_6H_3(NO_2)_2$-2,4 | 45.5 | 5.3 | 66.2 | — | — | — |

To study the effect of acid on the hydrolysis rate we ran an acid hydrolysis in the presence of HCl. The concentrations of the reactants were as follows: ester 0.00256 g-mole/liter, and acid 0.0033 g-mole/liter (which corresponds to 0.2502 g of 2,4-dinitrophenyl benzenesulfonate and 0.00365 g of HCl in a 30-ml sample). A parallel hydrolysis in the absence of acid was run at the same time. In the first case 9.65 ml of KOH (of which 6.85 ml was consumed in the neturalization of the original acid) was consumed in the titration of the acids, and in the second case 3.9 ml of KOH (0.0188 N solution) was consumed. The heating was for 45 hours in flasks fitted with reflux condensers. The titration results indicate that the hydrolysis rate not only does not increase in the presence of HCl, but is even hindered somewhat, since in this length of time the ester suffered hydrolysis to the extent of 33% under acidic hydrolysis conditions, and to the extent of 40% when aqueous hydrolysis conditions were employed.

## DISCUSSION OF RESULTS

From Table 4 it follows that the introduction of several nitro groups into either the acid or the alcohol component leads to a substantial increase in the rate of alkaline hydrolysis when compared with the mononitro-substituted esters. An especially noticeable increase in the hydrolysis rate is observed when two nitro groups are introduced into the phenol. The same rule that we had observed earlier [2, 3] is manifested here: the effect of electronegative substituents, transmitted through the benzene ring and the ester oxygen with free p-electrons, is condiderably greater than the effect of these same substituents, transmitted through the benzene ring directly to the sulfur atom.

The observed increase in the hydrolysis rate can be regarded as being due to p$\pi$-conjugation [11], since in the presence of inductive effects alone the action of the oxygen atom should lead to a weakening of the influence exerted by the nitro groups due to their remoteness from the sulfur atom.

To compare the influence exerted by two nitro groups, found in the benzenesulfonic acid, with the influence of the same groups in the phenol, it proves expedient to calculate the relative transmission coefficients of the electronic effects of substituents, found at different ends of the system, from the ratios of the hydrolysis rate constants of phenyl 2,4-dinitrobenzenesulfonate ($k_2$) to the unsubstituted phenyl benzenesulfonate ($k_1$) and that of 2,4-dinitrophenyl benzenesulfonate ($k_3$) to the unsubstituted phenyl benzenesulfonate ($k_1$): $f_1 = \frac{k_2}{k_1} = \frac{183}{0.06} = 3050$; $f_2 = \frac{k_3}{k_1} = \frac{880}{0.06} = 14300$; $f_2 : f_1 = 14300 : 3050 = 4.7$. In a similar manner for the p-mononitro-substituted derivatives: $f_3 = \frac{k_4}{k_1} = \frac{679}{0.06} = 113$; $f_4 = \frac{k_5}{k_1} = \frac{15.9}{0.06} = 265$; $f_4 : f_3 = 265 : 114 = 2.3$. Larger values of $f_4$ when compared with $f_3$ can serve as a quantitative measure of the p$\pi$-conjugation that exists in the esters of a substituted phenol and benzenesulfonic acid.

A large increase in $f_2$ when compared with $f_1$ is due to the effect of two factors: first, the presence of p$\pi$-conjugation, and second, the presence of an ortho-effect in the ester of 2,4-dinitrobenzenesulfonic acid and phenol. The latter is also supported by the large increase in the activation energy of hydrolysis (up to 7000 cal) in the case of the ester of 2,4-dinitrobenzenesulfonic acid and phenol when compared with the ester of benzenesulfonic acid and 2,4-dinitrophenol.

The effect exerted by the positions of the nitro groups in one benzene ring on the hydrolysis rate of aryl sulfonates may be followed on the phenyl esters of the 2,4- and 3,5-dinitrobenzenesulfonic acids: the first ester is saponified much more rapidly than the second. This indicates that the conjugation effect exerts a greater influence on the rate with which aryl sulfonates hydrolyze than does the inductive effect.

In contrast to the phenyl and tolyl benzenesulfonates, the dinitrophenyl benzenesulfonates are hydrolyzed by water (Table 5). The aqueous hydrolysis rate of the aryl sulfonates is considerably slower than that of the corresponding ethyl sulfonates [10]. The mononitro-substituted aryl sulfonates are not hydrolyzed by water, with the exception of the ester of benzenesulfonic acid and o-nitrophenol. The introduction of several nitro groups increases the aqueous hydrolysis rate substantially, in which connection an interesting rule is observed: the ester of 2,4-dinitrophenol and benzenesulfonic acid is hydrolyzed to the extent of 46%, while in the same length of time the ester of 2,4-dinitrobenzenesulfonic acid and phenol is hydrolyzed to the extent of 4%. A similar phenomenon is observed when a third nitro group is introduced into either the phenol or the sulfonic acid. The ester of 2,4-dinitrobenzenesulfonic acid and o-nitrophenol is hardly hydrolyzed by water, whereas the esters of o-nitrobenzenesulfonic acid and o-chlorobenzenesulfonic acid with 2,4-dinitrophenol show the most rapid saponification of all of the esters examined. Consequently, an o-nitro group in the phenol facilitates both the aqueous and the alkaline hydrolysis of aryl sulfonates. This can happen in two cases: 1) both processes proceed by the same mechanism — with rupture of the bond at the phenoxy group, and 2) the aqueous hydrolysis proceeds by a pseudoionic mechanism with rupture of the bond at the phenyl radical. The presence of some analogy between the aryl sulfonates, containing two nitro groups in the phenol, and the ethyl sulfonates (hydrolyzed by water and alkalies, and not hydrolyzed by acid) speaks in favor of the second mechanism. It is quite probable that a large increase in the acidic properties of the alcohol component in dinitro-substituted aryl sulfonates makes it possible for rupture to occur at both of the bonds of the ester oxygen.

## SUMMARY

1. We synthesized 6 dinitro-substituted aryl sulfonates and studied their alkaline and aqueous hydrolysis rates. The experimental results thus obtained were compared with the earlier-obtained data on the hydrolysis rates of nitro-substituted aryl sulfonates.

2. That the aqueous hydrolysis of aryl sulfonates is possible was established for the first time. The esters

most easily hydrolyzed by water are the esters of 2,4-dinitrophenol with the acids: 2-nitrobenzenesulfonic acid, 2-chlorobenzenesulfonic acid and benzenesulfonic acid.

## LITERATURE CITED

[1] R. V. Vizgert, Ukrain. Chem. J. 20, 272 (1954).

[2] R. V. Vizgert and E. K. Savchuk, J. Gen. Chem. 26, 2268 (1956).*

[3] R. V. Vizgert, J. Gen. Chem. 28, 1873 (1958).*

[4] C. A. Bunton and Y. F. Frei, J. Chem. Soc. 1951, 1872.

[5] G. Georgescu, Zbl. 1900, I, 543.

[6] A. I. Kiprianov and A. I. Tomachev, J. Gen. Chem. 27, 486 (1957).*

[7] C. Suter, Chemistry of Organic Sulfur Compounds [Russian translation] (IL, 1951), Chapter V, p. 372.

[8] Ia. P. Berkman and R. V. Vizgert, Ukrain. Chem. J. 20, 264 (1954).

[9] K. Hess and Frahm, Ber. 71, 2627 (1938).

[10] R. V. Vizgert and E. K. Savchuk, J. Gen. Chem. 26, 2261 (1956).*

[11] L. M. Litvinenko, R. S. Cheshko and A. D. Gofman, J. Gen. Chem. 27, 758 (1957).*

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# REACTIONS OF AROMATIC SULFONIC ACID ESTERS

## VII. ARYLATING PROPERTIES OF DINITROPHENYL BENZENESULFONATES

R. V. Vizgert and Ia. P. Berkman

It can be considered as established that in nucleophilic substitution reactions, as in reactions with water, alkalies, ammonia and amines, the aryl sulfonates show a similarity to carboxylic acid esters. All of these reactions proceed by a mechanism involving acyl-oxygen fission and the alcohol radical is not cleaved from its oxygen atom [1-11].

In contrast to the aryl sulfonates and carboxylic acid esters, the alkyl sulfonates behave as alkylating agents [12-16], for which reason in the reaction with water, ammonia and amines, the bond rupture occurs at the alkyl. It would be difficult to expect a mechanism involving alkyl-oxygen fission for aryl sulfonates, since here the oxygen is firmly bound to the aromatic ring. However, in the preceding paper we had established that the dinitrophenyl benzenesulfonates show a similarity to alkyl sulfonates in that they are hydrolyzed by water and alkalies, and are not hydrolyzed by acids. It could be assumed that this analogy will also appear in other nucleophilic substitution reactions. In order to verify such an assumption we ran a series of experiments in which the reactions of the dinitrophenyl esters of benzenesulfonic acid, p-chlorobenzenesulfonic acid and o-nitrobenzenesulfonic acid with ammonia, aromatic amines, potassium thiocyanate and potassium iodide were studied.

### EXPERIMENTAL

The reaction of the esters with nucleophilic reagents was run in 90% alcohol. Aqueous alcohol solutions of the 2,4-dinitrophenyl esters of benzenesulfonic acid (1), p-chlorobenzenesulfonic acid (2) and o-nitrobenzenesulfonic acid (3) were heated under reflux for 40 minutes, with the amines: aniline, p- and o-toluidine, p-anisidine, dimethyl- and diethyl-p-phenylenediamine, and $\alpha$-naphthylamine.

2,4-Dinitrodiphenylamine. A mixture of 1.08 g of 2,4-dinitrophenyl benzenesulfonate and 0.6 g of aniline was dissolved in 25 ml of 90% alcohol and the solution heated under reflux for 40 minutes. The solution was yellow at first, then it gradually turned red, and by the end of heating it was completely red. Half of the alcohol was distilled off, and the remaining solution on cooling deposited large red needles, which were filtered and washed with water. Recrystallization from alcohol gave 0.774 g (90%) of 2,4-dinitridiphenylamine. M. p. 154-156°. The aqueous filtrate was evaporated to give first 0.044 g (7.3%) of 2,4-dinitrophenol, and then 0.743 g (88%) of the aniline salt of benzenesulfonic acid. Consequently, the reaction goes with bond rupture at the aryl radical to the extent of 90% and with rupture at the phenoxy group to the extent of 7%. In subsequent reaction of aryl sulfonates with amines only the diphenylamines were isolated, and the direction of reaction was judged by their yield. The reactants – ester (0.0033 g-mole) and amine – were taken in a 1 : 2 ratio. In all cases, with the exception of p-nitroaniline, orange-red precipitates of variable hue, corresponding to the substituted dinitrodiphenylamines, were obtained in good yield (70-90%).

When 2,4-dinitrophenyl benzenesulfonate was reacted with ammonia under the indicated conditions we obtained only 2,4-dinitrophenol and benzenesulfonamide, i.e., the reaction goes with bond rupture at the phenoxy group. The passage of dry ammonia into a boiling solution of 1.08 g of 2,4-dinitrophenyl benzenesulfonate in 20 ml of benzene gave the ammonium salt of benzenesulfonic acid (0.4 g) and from the solution we isolated 0.37 g (60%) of 2,4-dinitroaniline, 0.05 g of benzenesulfonamide and 0.2 g of dinitrophenol.

Reaction of the esters with KCNS and KI was run under more drastic conditions. The aqueous alcohol solution of ester (0.0033 g-mole)and KCNS or KI (1 : 1 ratio) was heated for 18 hours on the water bath at 80°. On conclusion of reaction the alcohol was distilled off. The aqueous solution with precipitate was filtered and the precipitate washed with water. The amount of $CNS^-$ or $I^-$ ions in the filtrate was determined by titration, which could serve as an indirect indication of the reaction course.

2,4-Dinitrothiocyanobenzene. A mixture of 1.23 g of 2,4-dinitrophenyl o-nitrobenzenesulfonate and 0.32 g of KCNS was dissolved in 25 ml of 90% alcohol. The reaction was run the same as indicated above. The aqueous filtrate was collected, diluted to 250 ml, and 50 ml aliquots taken for titration (0.6 ml of 0.1-N $AgNO_3$ was consumed). Titration showed that 80% of the KCNS had reacted. The precipitate on the filter was shaken with 10% $Na_2CO_3$ solution, then extracted with chloroform, and the isolated crystals recrystallized from alcohol. We obtained 0.6 g (80%) of 2,4-dinitrothiocyanobenzene. M.p. 136-138°.

The reaction with KI was run in a similar manner. Here 70% of the KI reacted, but we were unable to obtain any 2,4-dinitroiodobenzene, and only 2,4-dinitrophenol (0.59 g, 60%) was isolated from the precipitate and distilled alcohol. Apparently, the 2,4-dinitroiodobenzene was converted to 2,4-dinitrophenol.

All of the indicated reactions were run with esters (1), (2) and (3), which gave similar reaction products in close yields. The experimental results are given in the table.

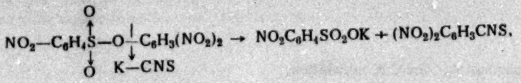
TABLE

Reaction of 2,4-Dinitrophenyl o-Nitrobenzenesulfonate With Ammonia, Aromatic Amines, KCNS and KI

| Reagent | Reaction product $R = 2,4\text{-}(NO_2)_2C_6H_3$ | Yield | | Melting point |
|---|---|---|---|---|
| | | g | % | |
| $NH_3$ | $RNH_2$ | 0.370 | 60 | 180—182° |
| $C_6H_5NH_2$ | $RNHC_6H_5$ | 0.774 | 90 | 153—155 |
| $p\text{-}CH_3C_6H_4NH_2$ | $RNHC_6H_4CH_3\text{-}p$ | 0.773 | 85 | 134—135 |
| $\alpha\text{-}C_{10}H_7NH_2$ | $RNHC_{10}H_7$ | 0.820 | 80 | 190—191 |
| $o\text{-}CH_3C_6H_4NH_2$ | $RNHC_6H_4CH_3\text{-}o$ | 0.682 | 75 | 125—126 |
| $p\text{-}CH_3OC_6H_4NH_2$ | $RNHC_6H_4OCH_3\text{-}p$ | 0.768 | 80 | 139—140 |
| $p\text{-}(CH_3)_2NC_6H_4NH_2$ | $RNHC_6H_4N(CH_3)_2\text{-}p$ | 0.705 | 70 | 166—167 |
| $p\text{-}(C_2H_5)_2NC_6H_4NH_2$ | $RNHC_6H_4N(C_2H_5)_2\text{-}p$ | 0.748 | 68 | 107—110 |
| $p\text{-}NO_2C_6H_4NH_2$ | No reaction | | | |
| KCNS | RCNS | 0.600 | 80 | 137—139 |
| KI | Not isolated | | | |

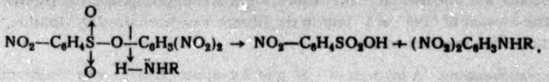
The experimental data indicate that the reactions with aromatic amines go in good yields if nucleophilic substituents are present in the benzene ring, increasing the basicity of the amino group, i.e., its electron-donor properties. The introduction of an electrophilic substituent apparently reduces the electron-donor properties of the amino group to such an extent that the reaction with p-nitroaniline failed to go. Consequently, nucleophilic substitution reactions in the case of aryl sulfonates can go only if agents with a large nucleophilic affinity are present [17].

All of the executed reactions certainly indicate alkyl-oxygen fission. It is possible to assume that alkyl-oxygen fission does not necessarily proceed with the formation of free carbonium ions, but instead can be accomplished by pseudoionic mechanisms, where fission of the intermediately formed reaction complexes should proceed at the most polar bonds [18]. In the esters of 2,4-dinitrophenol, in the presence of electron-donor reagents, such a bond is the C−O bond, and not the S−O bond. The reaction with KCNS may be depicted by the scheme:



$$NO_2{-}C_6H_4\overset{\overset{O}{\uparrow}}{\underset{\underset{O}{\downarrow}}{S}}{-}O\underset{\underset{K-CNS}{\downarrow}}{\mid}C_6H_3(NO_2)_2 \rightarrow NO_2C_6H_4SO_2OK + (NO_2)_2C_6H_3CNS.$$

Apparently preliminary polarization of the H—NHR bond occurs in the case of ammonia and amines. Here the arylation mechanism may be depicted by the scheme



$$NO_2-C_6H_4\overset{\overset{O}{\uparrow}}{\underset{\underset{O}{\downarrow}}{S}}-O\underset{\underset{H-\ddot{N}HR}{\downarrow}}{\overset{|}{-}}C_6H_3(NO_2)_2 \rightarrow NO_2-C_6H_4SO_2OH + (NO_2)_2C_6H_3NHR.$$

## SUMMARY

The reaction of the 2,4-dinitrophenyl esters of benzenesulfonic acid, p-chlorobenzenesulfonic acid and o-nitrobenzenesulfonic acid with ammonia, aromatic amines, KCNS and KI was studied. The corresponding substituted dinitrodiphenylamines and 2,4-dinitrothiocyanobenzene were obtained. The isolated reaction products indicate that the esters of 2,4-dinitrophenol and substituted benzenesulfonic acid suffer alkyl-oxygen fission.

## LITERATURE CITED

[1] M. Polanyi and A. Szabo, Trans. Faraday Soc. 30, 508 (1934).

[2] E. Tomila and C. Hinshelwood, J. Chem. Soc. 1801 (1938).

[3] J. Day and C. Ingold, Trans. Faraday Soc. 37, 689 (1941).

[4] M. Gordon, J. Miller and J. Day, J. Am. Chem. Soc. 70, 1946 (1948).

[5] R. V. Vizgert, Ukrain. Chem. J. 20, 272 (1954).

[6] Ia. P. Berkman and R. V. Vizgert, Ukrain. Chem. J. 20, 264 (1954).

[7] R. V. Vizgert, J. Gen. Chem. 28, 1873 (1958).*

[8] R. V. Vizgert and E. K. Savchuk, J. Gen. Chem. 26, 2261, 2268 (1956).*

[9] R. Otto, Ber. 19, 1832 (1886).

[10] K. Freudenberg and H. Hess, Lieb. Ann. 448, 121 (1926).

[11] D. Klamann, Ann. 583, 63 (1953).

[12] L. Autenrieth and Bernheim, Ber. 37, 3803 (1904).

[13] F. Ullmann and Nadai, Ber. 41, 1871 (1908).

[14] V. M. Rodionov, Bull Soc. Chim. 45, 109 (1929).

[15] L. Demeny, Rech. trav. chim. 50, 60 (1931).

[16] G. Kenner and M. Murray, J. Chem. Soc. 1950, 406.

[17] V. Stimson, J. Chem. Soc. 1955, 2010.*

[18] C. Bunton and A. Konasiewicz, J. Chem. Soc. 1955, 1354.

[19] V. Stimson, J. Chem. Soc. 1955, 2673.

[20] T. Kharkharov, J. Gen. Chem. Suppl. II, 1663 (1953).

[21] N. Deno and M. Newman, J. Am. Chem. Soc. 73, 1920 (1951).

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# THE THERMAL ADDITION OF TRICHLOROSILANE TO DIOLEFIN HYDROCARBONS

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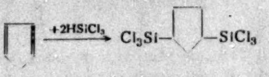
In a previous work [1] we investigated the reaction of the thermal addition of trichlorosilane to monoolefin hydrocarbons. We later considered it of interest to extend this reaction to various diolefin hydrocarbons. There are certain references in literature [2-8], mainly dealing with patents, of the possibility of carrying out both thermal [2-6] and catalytic [1-8] addition reactions of trichlorosilane and diolefin hydrocarbons. We did not succeed in adding trichlorosilane to a number of diolefins containing conjugated double bonds in the presence of organic peroxides or under the influence of ultraviolet light because these agents caused polymerization of the initial hydrocarbons which took place much more rapidly than the addition of $HSiCl_3$ to the double bond. In the majority of instances, however, when the reaction was carried out in the absence of catalysts at increased temperature and pressure, the desired result was obtained.

We carried out the thermal addition reaction of trichlorosilane and aliphatic or alicyclic hydrocarbons containing two isolated or conjugated double bonds in an autoclave at 280° under the same conditions as in the case of monoolefins [1]. In this process it was found that 1,5-hexadiene containing isolated double bonds reacts with excess trichlorosilane in a similar way to monoolefin hydrocarbons, giving 70% yield of 1,6-bis (trichlorosilyl)-hexane according to the system:

$$CH_2{=}CH(CH_2)_2CH{=}CH_2 \xrightarrow{+2HSiCl_3} Cl_3Si(CH_2)_6SiCl_3.$$

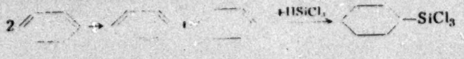
The structure of the latter, established by the combination dispersion-spectrum of light, shows that even with the presence of two isolated double bonds in the hydrocarbon molecule the addition takes place according to Farmer's rule [9], i.e., the $SiCl_3$ group combines with the most hydrogenated carbon atom having a double bond.

1,3-Cyclopentadiene which contains conjugated double bonds also adds smoothly and readily to trichlorosilane giving a 45% yield of 1,3-bis(trichlorosilyl)cyclopentane



This compound was obtained with a 28.5% yield by the addition of trichlorosilane to 4,7-methano-4,7,8,9-tetrahydroindene (dicyclopentadiene). Its formation evidently precedes the thermal depolymerization of dicyclopentadiene to cyclopentadiene. The formation, with a low yield, of a mixture of isomeric addition products of one and two molecules of trichlorosilane and a molecule of dicyclopentadiene was also noted.

The reaction of trichlorosilane with 1,3-cyclohexadiene led unexpectedly to the formation of cyclohexyltrichlorosilane and benzene. This can be explained by the fact that under the reaction conditions 1,3-cyclohexadiene undergoes "irreversible catalytic conversion" (see [10]) into benzene and cyclohexene* to which trichlorosilane is also added according to the system:



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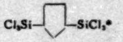
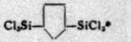
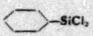
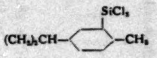
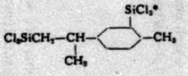
* When cyclohexadiene is heated in an iron autoclave at 300° for 6 hours benzene and cyclohexane are formed [11].

TABLE 1

Addition Products of Trichlorosilane and Diolefins

| Initial diolefin | Addition product | Yield of unpurified product (as % of initial diolefin) | Boiling point (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ | $\left(n_F^{20} - n_C^{20}\right) \cdot 10^4$ | M |  | Cl |  | Si |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  |  | found | calc. | found | calc. | found | calc. |
| 1,5-Hexadiene | $Cl_3Si(CH_2)_6SiCl_3$ | 70 | 281.0° (760) | 1.327 | 1.4759 | 94.5 | 349.3, 352.2 | 353.08 | 60.37, 60.37 | 60.25 | 15.60, 15.38 | 15.91 |
| 1,3-Cyclopentadiene |  | 45 | 143.5 (13) | 1.455 | 1.4997 | 101 | 343.1, 340.4 | 337.04 | 63.12, 63.27 | 63.12 | 16.75, 16.19 | 16.67 |
| Dicyclopentadiene |  | 28.5 | 151.5 (22) | 1.449 | 1.4999 | 102 | 323.9, 329.9 | 337.04 | 63.46, 63.62 | 63.12 | 16.93 | 16.67 |
| 1,3-Cyclohexadiene |  | 45 | 91.5 (11) | 1.229 | 1.4797 | 94.5 | 214.6, 213.4 | 217.61 | 49.16, 49.38 | 48.88 | 13.37, 13.58 | 12.91 |
| Dipentene |  | 68 | 139.5 (17) | 1.154 | 1.4890 | 97.5 | 268.5, 270.0 | 273.72 | 39.35, 39.46 | 38.86 | 10.09, 10.94 | 10.26 |
|  |  | 20 | 202.0 (17.5) | 1.298 | 1.5080 | 103.5 | 408.0, 414.6 | 407.17 | 51.64, 50.68 | 52.25 | 13.60, 13.42 | 13.80 |

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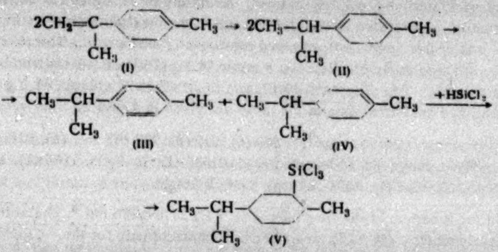
* The mutual location of the trichlorosilyl groups in the addition product is hypothetical.

In the thermal addition of trichlorosilane to D,L-1-methyl-4-isopropenyl-1-cyclohexene (dipentene) (I), methyltrichlorosilane (V) and cymene (III) are formed as well as the normal addition product of two molecules of trichlorosilane (yield 20%). The reaction mechanism of their formation may be represented in the following manner:



Dipentene (I) isomerizes to α-terpinene (II) as a result of the migration of the double bond from the isopropenyl group into the ring. As in the case of cyclohexadiene the α-terpinene undergoes "irreversible catalytic conversion" to cymene (III) and carbomenthene (IV),* which also adds a molecule of trichlorosilane.

Table 1 gives the addition products obtained from trichlorosilane and the five investigated diolefins their yields, physical properties and the data from determination of the molecular weight. The results of our investigations on the thermal addition of trichlorosilane and aliphatic diolefins with conjugated double bonds will be given in another work.

TABLE 2

Physical Constants of the Initial Diolefins

| Diolefin | Boiling point (at 760 mm) | $d^{20}_4$ | $n^{20}D$ | $(n^{20}F - n^{20}C) \cdot 10^4$ |
|---|---|---|---|---|
| 1,5-Hexadiene . . . . . . . . . . | 59.4* | 0.6930 | 1.40381** | 100.9 |
| 1,3-Cyclopentadiene . . . . . . | 40.3 | – | 1.4437 | 127.5 |
| 1,3-Cyclohexadiene . . . . . . | 80.5 | 0.8408 | 1.4749 | 130 |
| Dipentene . . . . . . . . . . . . . | 176.6 | – | 1.4738 | 111 |
| Dicyclopentadiene . . . . . . . | 54 (14 mm)*** | – | 1.5012 | 114 |

## EXPERIMENTAL

Initial reagents. Trichlorosilane [1], 1,5-hexadiene [14], 1,3-cyclopentadiene [15] and 1,3-cyclohexadiene [16] were obtained and purified by methods described in literature. Dicyclopentadiene was washed with a solution of KOH and then with water; it was dried over $CaCl_2$ and was twice fractionally distilled under vacuum over metallic sodium. The physical properties of the diolefins corresponding to the most reliable literature data, are given in Table 2. Diolefins with conjugated double bonds were introduced into the reaction immediately after they were obtained.

Investigation procedure. All the reactions were carried out in a 250 ml steel autoclave equipped with a copper obturator and a manometer. The autoclave was heated in an oil thermostat at 280 ± 5°. The course of the reaction was controlled according to the pressure in the autoclave. Heating was carried out until the drop in the pressure had completely ceased. The liquid reaction products were distilled from a flask with an arborescent fractionating column at ordinary or reduced pressure after which they were purified by distillation in a fractionating column with an efficiency of 20 theoretical plates. The purified products were immediately sealed in ampoules and in all operations carried out on them, measures were adopted to prevent the penetration of atmospheric moisture. The analytical procedure and the method of determining the physical constants have been described by us previously [1].

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* The thermal conversion of dipentene (limonene) to cymene and carbomenthene in the presence of copper is described in literature [12].

** $n^{20}C$ 1.40087.

*** M.p. 32.5°.

The addition of trichlorosilane to 1,5-hexadiene. A mixture of 24.6 g of 1,5-hexadiene and 108.4 g of trichlorosilane was heated in an autoclave at 280° for 10 hours. The maximum pressure in the autoclave (45 atm) fell to 10 atm by the end of this period and remained subsequently unchanged. The reaction product (127 g), a yellow-green liquid, was fractionally distilled. As a result 74.1 g (70%) of 1,6-bis(trichlorosilyl)hexane with a b.p. of 278-286° was obtained. After repeated distillation in an efficient column, 54.0 g of the pure substance was obtained; the constants and analytical data of the latter are given in Table 1.

Combined dispersion spectrum $\Delta\nu$ cm$^{-1}$:* 169 (6), 212 (0), 232 (3), 271 (4), 318 (1), 442 (10), 469 (8), 500 (2), 564 (3 long), 590 (3 long), 762 (6 broad), 997 (1), 1046 (1), 1069 (1), 1105 (1), 1192 (2 long), 1247 (1 long), 1307 (3), 1400 (3), 1443 (6), 2861 (3), 2900 (2 long), 2936 (2 long).

The absence in the spectrum of the frequency $\nu$ (C − H) 2970-2990 cm$^{-1}$, characteristic for the $-CH_3$ group and the presence of the doublet $\nu$ (Si − Cl), 564,590 cm$^{-1}$, characteristic for the $-CH_2-SiCl_3$ group, undoubtedly shows that the addition product is 1,6-bis(trichlorosilyl)hexane. In addition to the latter, 5 g of a substance was obtained which had a b.p. of 182-192°, contained 49% of hydrolyzable chlorine and decolorized a solution of bromine in chloroform. It must be assumed that this was 5-hexenyltrichlorosilane.

The addition of trichlorosilane to 1,3-cyclopentadiene. 13.2 g of cyclopentadiene and 67.7 g of trichlorosilane were heated in an autoclave at 280° for 15 hours. The maximum pressure of 31 atm at this temperature fell during a period of 12 hours to 15 atm and subsequently remained unaltered. As a result of the fractional distillation of the autoclave contents (74 g) 16 g of the initial trichlorosilane and 30.4 g (45%) of bis(trichlorosilyl)-cyclopentane with a b.p. of 143-149° (16 mm) were obtained. After redistillation under vacuum in a column it had the constants given in Table 1.

The reaction of trichlorosilane with dicyclopentadiene. 26.4 g of dicyclopentadiene and 135.5 g of trichlorosilane were heated in an autoclave at 280° for 19 hours. The maximum pressure in the autoclave was 38 atm, the minimum was 26 atm. As a result of the fractional distillation of the reaction mixture (157 g) about 50 g of excess trichlorosilane and 38.4 g (28.5%) of bis(trichlorosilyl)cyclopentane with a b.p. of 122-127° (6 mm) were obtained. After redistillation it had constants (Table 1) similar to the constants of this compound obtained from cyclopentadiene. In addition to this compound, 9.1 g of the addition product of one molecule of trichlorosilane and a molecule of dicyclopentadiene (evidently a mixture of isomeric trichlorosilyl-4,7-methanohexahydroindenes) was obtained; the latter was a thick yellow liquid with a b.p. of 200-230° (10 mm).

Found %: Cl 39.95, 40.09. $C_{10}H_{13}Cl_3Si$. Calculated %: Cl 39.74.

A small amount of a substance with a b.p. of 280-300° (6 mm), containing silicon and hydrolyzable chlorine, was obtained from the higher-boiling residue. It must be assumed that this was the addition product of two molecules of trichlorosilane and a molecule of dicyclopentadiene (a mixture of isomeric bis(trichlorosilyl)-4,7-methanooctahydroindenes).

The reaction of trichlorosilane with 1,3-cyclohexadiene. 16.0 g of cyclohexadiene and 81.3 g of trichlorosilane were heated in an autoclave at 280°. 1.5 hours after the commencement of heating the pressure increased to 46 atm and after 0.5 hours began to fall, reaching 30 atm after 12 hours. Further heating for 6 hours did not result in a change in the pressure. The reaction mixture obtained (95.0 g of a green fluorescent liquid) was fractionally distilled. As a result 49.0 g of the initial trichlorosilane and 9.0 g of a substance with a b.p. of 50-85° were obtained. The latter was washed with water and a solution of alkali, dried over $CaCl_2$ and distilled over sodium. A main fraction with a b.p. of 78-82° was obtained and identified as benzene in the form of m-dinitrobenzene with an m.p. of 88-89°. A mixed melt with commercial m-dinitrobenzene showed no depression of the melting point.

The higher-boiling residue was distilled under vacuum (the distillation was accompanied by intense frothing).

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* The combined dispersion spectrum was determined by V. A. Kolesova (see [17]) to whom we wish to express our gratitude.

As a result 10.0 g of a substance was obtained which had a b.p. of 88-93°, did not add bromine and after redistillation had the constants given in Table 1. These constants agree well with the literature data for cyclohexyltrichlorosilane [1, 17]: b.p. 206.5° (760 mm), 90° (10 mm), $d^{20}_4$ 1.222, $n^{20}$D 1.4774. The data of the analysis and the molecular weight determination also confirm that the substance obtained was cyclohexyltrichlorosilane.

The reaction of trichlorosilane with dipentene. A mixture of 27.2 g of dipentene and 67.7 g of trichlorosilane was heated in an autoclave at 280° for 20 hours. After several hours the maximum pressure of 25 atm established fell to 20 atm, after which it remained constant the whole time. As a result of the fractional distillation of the mixture of reaction products (93.0 g), firstly at atmospheric pressure and then under vacuum, 13.5 g of the initial trichlorosilane with a b.p. of 32-37° and three principal higher-boiling fractions were obtained: 1st fraction 56-62° (10 mm), 9.2 g; 2nd, 124-130° (8 mm), 18.5 g; 3rd, 166-174° (7 mm), 16.5 g. The residue in the flask had a b.p. above 250° (5 mm).

As a result of the nitration of the 1st fraction, 2,6-dinitro-p-cymene with an m.p. of 54° was obtained (the identity was proven by a mixed melt). After redistillation the 2nd fraction had the constants given in Table 1. This substance does not add bromine and according to the analytical data and the molecular weight determination (Table 1) corresponds to the formula $C_{10}H_{19}SiCl_3$, i.e., 1-methyl-4-isopropyl-trichlorosilylcyclohexane. The yield was 68%. From the analytical data and the molecular weight determination (Table 1) the 3rd fraction corresponds to the addition product of two molecules of trichlorosilane and a molecule of dipentene (yield 20%).

## SUMMARY

The thermal addition of trichlorosilane to diolefin hydrocarbons with isolated and conjugated double bonds was investigated. In the first instance the addition reaction takes place normally according to the law of free radical addition. The addition of trichlorosilane to 1,3-cyclopentadiene and dicyclopentadiene leads mainly to the formation of bis(trichlorosilyl) cyclopentane. The reaction of trichlorosilane with 1,3-cyclohexadiene and also to a considerable extent with dipentene is abnormal, leading to the formation of the addition product of the corresponding cyclomonoolefine, the product of the "irreversible catalytic conversion" of the initial hydrocarbon. 6 addition products of trichlorosilane and diolefins are described, the majority of them being hitherto unknown.

## LITERATURE CITED

[1] M. G. Voronkov, N. G. Romanova and L. G. Smirnova, Chem. Listy, 52, 640 (1958).

[2] A. J. Barry, L. De Pree, J. W. Gilkey and D. E. Hook, J. Am. Chem. Soc., 69, 2916 (1947).

[3] British Patent 633732 (1949); Ch. A., 45, 3409 (1951).

[4] American Patent 2545780 (1951); Ch. A., 45, 7590 (1951).

[5] American Patent 2624721 (1953); Ch. A., 47, 3613 (1953).

[6] American Patent 2665287 (1954); Ch. A., 49, 1105 (1955).

[7] American Patent 2570462 (1951); Ch. A., 46, 6141 (1952).

[8] American Patent 2533240 (1950); Ch. A., 45, 2261 (1951).

[9] E. H. Farmer, J. Soc. Chem. Ind., 66, 86 (1947).

[10] N. Zelinski and G. Pavlov, Ber., 66, 1420 (1933).

[11] B. B. Corson and V. N. Ipatieff, J. Am. Chem. Soc., 61, 1056 (1939).

[12] R. Ia. Levina, The Synthesis and Contact Catalytic Conversions of Unsaturated Hydrocarbons, Moscow State University Press (1949).*

[13] S. Komatsu and M. Kurata, Zbl., 1928, II, 1326.

[14] Synthesis of Organic Compounds, Symp., 4, 147 (1953).*

[15] B. A. Kazanskii, E. M. Terent'eva, Syntheses of Organic Compounds, Symp. 1, Acad. Sci. USSR Press, 158 (1950); Synthesis of Organic Compounds, Symp. 4, 565 (1953).*

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*In Russian.

[16] Iu. A. Arbuzov, N. D. Zelinskii, and N. I. Shuikin, Bull. Acad. Sci. USSR, Div. Tech. Sci., 1945, 163.

[17] V. A. Kolesova, M. G. Voronkov, Symp. Czechoslov. Chem. Works, 22, 851 (1957); Chem. Listy, 51, 686 (1957).

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# INVESTIGATIONS IN THE FIELD OF ALKOXYSILANES

## XII. HEXA-TERTIARY-BUTOXYCYCLOTRISILOXANE*

M. G. Voronkov, V. P. Davydova and A. N. Lazarev

Polydialkoxycyclosiloxanes $[(RO)_2SiO]_n$ have hitherto been obtained by a hydrolysis reaction [2-4].

$$n\,(RO)_2SiX_2 + nH_2O \rightarrow [(RO)_2SiO]_n + 2nHX,$$

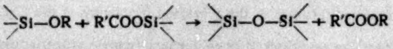
where

$$R = C_2H_5,\ C_4H_9;\ X = Cl,\ OC_2H_5,\ NH_2;\ n = 3\text{—}8.$$

We observed a very interesting instance of the formation of hexa-tertiary-butoxycyclotrisiloxane, previously unknown, by the intramolecular condensation of tri-tertiary-butoxyacetoxysilane in a medium of tertiary butyl alcohol** in the presence of sodium tertiary butylate according to the system

$$3(RO)_2Si(OR)OCOCH_3 \rightarrow [(RO)_2SiO]_3 + 3CH_3COOR, \text{where} R = C(CH_3)_3.$$

A reaction of this type with the formation of a siloxane bond as a result of the condensation of alkoxy- and aryloxysilanes



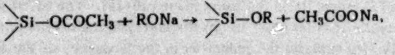
$$\gt Si\text{—}OR + R'COOSi\lt\ \rightarrow\ \gt Si\text{—}O\text{—}Si\lt + R'COOR$$

has hitherto been little known in the chemistry of organosilicon compounds [5].

It should be noted, however, that an analogous condensation of alkoxysilanes with acetates or acetoxysilanes with alkoxides of other elements has been fairly extensively described [6-8]. It is also of interest that the principal product of the above-mentioned reaction is the completely stable cyclic trisiloxane and not tetrasiloxane as might have been expected. This is undoubtedly due to the influence of the tertiary butoxy groups.

In contrast to octaethoxycyclotetrasiloxane, hexaethoxycyclotrisiloxane is obtained with difficulty and is extremely unstable [4].

We did not succeed in carrying out the condensation reaction of alkoxysilanes with acetoxysilanes in other examples. This is explained by the fact that the corresponding sodium alcoholate which catalyzes this reaction readily reacts with acetoxysilanes according to the system



$$\gt Si\text{—}OCOCH_3 + RONa \rightarrow\ \gt Si\text{—}OR + CH_3COONa,$$

as a result of which it is completely removed from the sphere of the reaction and the acetoxysilane is converted into the corresponding alkoxy derivative. In the case of tri-tertiary-butoxyacetoxysilane an analogous reaction with sodium tertiary butylate does not take place owing to steric hindrance.

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* For previous communication see [1].

** In the absence of $(CH_3)_3COH$ the reaction proceeds in a different direction.

The infrared absorption spectrum of hexa-tertiary butoxycyclotrisiloxane was investigated in the 700-400 $cm^{-1}$ region by means of a VIKS-MZ spectrometer with an NaCl prism. The sample was prepared by the method of pressing a disk (25 mm in diameter) from a mixture of 10 mg of the substance and 2 g of KBr [9]. The values of the frequencies obtained in the absorption spectrum of hexa-tertiary butoxycyclotrisiloxane (in $cm^{-1}$) are given below: 2975, ~1470 (db),* 1391, 1368, 1246, ~1210, 1193, 1131, 1084, 1046, 982, 914, 837, 824, 769, ~715 (b);* 702.

A band in the 3500 $cm^{-1}$ region, associated with the presence of traces of moisture in the KBr, is also present in the spectrum shown in Fig. 1.

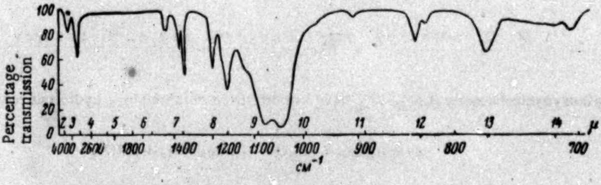

Fig. 1. Infrared absorption spectrum of hexa-tertiary butoxycyclotrisiloxane.
• – band of the water contained in KBr.

A hypothetical interpretation can be given for some of the bands observed. In the region of deformation vibrations of the $CH_3$ groups, a band of antisymmetrical vibration of 1470 $cm^{-1}$ and two bands of symmetrical vibrations of the $CH_3$ groups (1391 and 1368 $cm^{-1}$), characteristic of a tertiary butyl group, are present. Of the 1391 and 1368 $cm^{-1}$ bands the second is more intense, which is also typical of a $C(CH_3)_3$ group [10].

The 1246 $cm^{-1}$ band is attributed to the skeletal vibrations of the $C(CH_3)_3$ group, it being probable that the 914 $cm^{-1}$ band is also caused by the vibrations of this group. The intense 1084-1064 $cm^{-1}$ bands are associated with Si–O–Si and Si–O–C valence vibrations. It is possible that the 1193 $cm^{-1}$ band is included in the C – O vibrations although it is not out of the question that the existence of the 1246 and 1193 (or 1210) $cm^{-1}$ frequencies is caused by the frequently observed splitting of the vibration frequency of the $C(CH_3)$ group [10].

It is of interest to compare the spectrum of hexa-tertiary butoxycyclotrisiloxane with that of tetra-tertiary butoxysilane, previously investigated by us [11, 12]. The spectra show a considerable similarity (with the exception of the disappearance of the 1027 $cm^{-1}$ band, if it is not hidden by the edge of the stronger 1046 $cm^{-1}$ band) but the 831 $cm^{-1}$ band splits into two (837 and 824 $cm^{-1}$) and, in addition, a new, fairly intense 769 $cm^{-1}$ band appears. It should be noted that the band of Si–O–Si and Si–O–C vibrations in hexa-tertiary butoxycyclotrisiloxane consists of two further-removed components (1084 and 1064 $cm^{-1}$) than in tetra-tertiary-butoxysilane (1063 and 1053 $cm^{-1}$); its frequency is not only unreduced but is even somewhat increased.

In all the investigated alkyl- and arylsiloxanes the Si–O vibration band in the spectra of cyclotrisiloxanes is displaced toward the lower frequencies (1020 $cm^{-1}$) while in the spectra of cyclotetrasiloxanes and higher-membered siloxane rings this band lies in the 1050-1100 $cm^{-1}$ region, i.e., it differs little from the frequencies of linear siloxanes (Si–O–Si bonds) and alkoxysilanes (Si–O–C bonds) [10, 13]. It is natural to associate this fact with the differences in the structures of cyclic tri- and tetra siloxanes. According to data obtained by x-rays and the electron diffraction camera, cyclosiloxanes form, as a rule, a nonplanar unstressed ring [14, 15] and only in the case of cyclotrisiloxanes do all the Si and O atoms lie in the same plane [16-18]. The SiOSi angles in cyclotrisiloxanes are smaller than in the higher cyclosiloxanes (136° in hexamethylcyclotrisiloxane and 142.5° in octamethylcyclotetrasiloxane [14]); this evidently also explains the reduction in the frequency of the antisymmetrical vibration of the Si–O–Si bond. Since a reduction in the frequency of the Si–O vibrations, characteristic of cyclotrisiloxanes, is not found in the spectrum of hexa-tertiary butoxycyclotrisiloxane we believe it can be assumed that in this instance the SiOSi angles are close to the values of the angles in cyclotetrasiloxanes and aliphatic siloxane. An increase in the SiOSi angles in hexa-tertiary butoxycylotrisiloxane is only possible, however, as a result of a decrease in the OSiO angles which are usually close to those of a tetrahedron. It may be considered that such a reduction of the OSiO angle in the ring is due to the presence of two "spatially difficult" $OC(CH_3)_3$ groups added to each silicon atom. This corresponds to the ideas of Ingold and Thorpe [19] according to which as a result of mutual repulsion the gem substituents in a tetrahedral atom in a ring reduce the angle between two other valence bonds included in the ring.

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* Double.

** Broad.

## EXPERIMENTAL

Hexa-tertiary-butoxycyclotrisiloxane. 61.5 g of tri-tertiary butoxyacetoxysilane [20] was added dropwise with stirring to a boiling solution of 5.75 g of metallic sodium in 118.6 g of anhydrous tertiary butyl alcohol. After the boiling reaction mixture had been stirred for two hours, the volatile products (85 g with a b.p. of 25-33° at 25-30 mm) were distilled from the former under vacuum on an oil bath, the temperature of which had been raised to 150°. The voluminous dry residue left in the distillation flask was extracted with absolute ether. Well-formed white needles were deposited from the ethereal solution when it was evaporated; after recrystallization from alcohol the m.p. of the crystals was 135° (after sublimation under vacuum the m.p. was 136°).

Found %: C 50.72, 50.82; H 9.51, 9.59; Si 14.58, 14.54. M 571.5, 559.6. $C_{24}H_{54}O_9Si_3$. Calculated %: C 50.49; H 9.54; Si 14.45. M 570.96.

The yield of the pure substance was 11.4 g (30%). Tri-tertiary butoxyacetoxysilane did not give hexa-tertiary butoxycyclotrisiloxane on long boiling with tertiary butyl alcohol in the absence of sodium tertiary butylate and when the reaction mixture was distilled the initial reagents were obtained almost unchanged.

Attempt to synthesize $[(CH_3)_2SiO]_n$ from dimethyl-n-butoxyacetoxysilane. a) 9.5 g of dimethyl-n-butoxyacetoxysilane [21] and 0.5 g of sodium n-butylate freed from traces of butanol, were heated to boiling for 5 hours with a reflux condenser. After the reaction mixture had been distilled, 9.0 g of unchanged initial dimethyl-n-butoxyacetoxysilane with a b.p. of 173-174° (757 mm), $n^{20}D$ 1.4015 was obtained.

b) 19.0 g of dimethyl-n-butoxyacetoxysilane was added dropwise with stirring to a boiling solution of 2.85 g of metallic sodium in 75 ml of n-butyl alcohol. After the reaction mixture had been boiled and stirred for two hours it was cooled and filtered. When the filtrate was distilled, 10.5 g (51%) of dimethyl-di-n-butoxysilane with a b.p. of 189-190° (765 mm), $d^{20}_4$ 0.8438, $n^{20}D$ 1.4051 was obtained. These constants agree well with literature data [22]: b.p. 186-188° (765 mm), $d^{20}_4$ 0.8434, $n^{20}D$ 1.4058. The ethereal extract of the filtered precipitate contained hardly any dissolved substances.

## SUMMARY

It was shown that in a medium of tertiary butyl alcohol and in the presence of sodium tertiary butylate, tri-tertiary butoxyacetoxysilane is converted into the previously unknown hexa-tertiary butoxycyclotrisiloxane. The infrared absorption spectrum of this compound was investigated and an interpretation of it was given, making it possible to draw certain conclusions regarding the ring structure.

## LITERATURE CITED

[1] V. P. Davydova and M. G. Voronkov, J. Gen. Chem. 28, 1879 (1958).*

[2] R. K. Iler, Ind. Eng. Ch. 39, 1348 (1947).

[3] T. Takatani, J. Chem. Soc. Japan, Pure Chem. Sect. 72, 765 (1951); 74, 890, 947 (1953).

[4] R. Okawara, S. Hotta, and T. Watase, J. Chem. Soc. Japan 28, 541 (1955); R. Okawara, S. Hotta, and T. Shimura, Bull. Chem. Soc. Japan 28, 541 (1955).

[5] K. A. Andrianov, N. N. Sokolov, and E. N. Khrustaleva, J. Gen. Chem. 26, 1102 (1956);* H. Post, C. H. Hofrichter, J. Org. Ch. 5, 443 (1940).

[6] F. A. Henglein, Z. angew. Ch. 66, 566 (1954); Chem. Techn. 7, 210 (1955); Chimia 9, 187 (1955); Makrom. Chem. 15, 177 (1955); 18-19, 102 (1956); 22, 103 (1957).

[7] K. A. Andrianov, L. M. Volkova, Bull Acad. Sci. USSR, Div. Chem. Sci. 1957, 303.*

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*Original Russian pagination. See C.B. translation.

[8] M. L. Darashkevich, Dissertation, "The Preparation of New Types of Silicates on the Basis of Organosilicon Compounds," Moscow (1957);* Theses of Reports of the Sci-Tech. Con. of MKhTI, 67 (1957).

[9] M. M. Stimson and M. J. O'Donnell, J. Am. Chem. Soc. 74, 1805 (1952).

[10] L.J. Bellamy, The Infrared Spectra of Complex Molecules, London – N.Y. (1956).

[11] A. N. Lazarev, M. G. Voronkov, Opt. and Spectr. 4, 180 (1958).

[12] M. G. Voronkov, A. N. Lazarev, A. K. Baigozhin, J. Gen. Chem. 26, 3072 (1956).*

[13] C. W. Young, P. C. Servais, C. C. Currie and M. J. Hunter, J. Am. Chem. Soc. 70, 3758 (1948).

[14] H. Steinfink, B. Post, and I. Fankuchen, Acta Cryst. 8 420 (1955).

[15] E. H. W. Aggarval and S. H. Bauer, J. Chem. Phys. Soc. 67, 2275 (1945).

[16] E. H. W. Aggarval and S. H. Bauer, J. Chem. Phys. 18, 42 (1950).

[17] W. L. Roth and D. Harker, Acta Cryst. 1, 34 (1948).

[18] G. Peironel, Chim. Industr. 36, 441 (1954).

[19] N. A. Domnin, The Structure of Cyclic Compounds in the Light of the Theory of Strain, United Sci-Tech. Press 164 (1936);* E. L. Eliel and M. S. Newman, Steric Effects in Organic Chemistry., N.Y., 117 (1956).

[20] B. N. Dolgov, V. P. Davydova and M. G. Voronkov, J. Gen. Chem. 27, 921 (1957).*

[21] B. N. Dolgov, V. P. Davydova and M. G. Voronkov, J. Gen. Chem. 27, 1593 (1957).*

[22] R. O. Sauer, J. Am. Chem. Soc. 68, 138 (1946).

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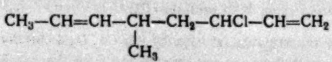
# INVESTIGATIONS IN THE FIELD OF CONJUGATED SYSTEMS

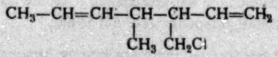
## XC. THE ADDITION OF 2-CHLORO-3-PENTENE TO DIVINYL*

A. A. Petrov, N. A. Razumova and M. L. Genusov

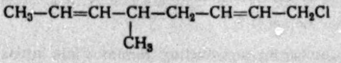
The reaction of 2-chloro-3-penten with divinyl is one of the simplest instances of a telomerization reaction with the participation of a haloid derivative of the allyl type and a diene hydrocarbon. In the first place, the possibility of the addition of two allyl isomers of the haloid derivative to the hydrocarbon is excluded in this instance because they are identical. Secondly, as a result of the symmetry of divinyl, the number of possible simple addition products with the composition $C_9H_{15}Cl$ is a minimum in this instance, being equal to 3 (I) – (III).



$$\mathrm{CH_3{-}CH{=}CH{-}\underset{\displaystyle CH_3}{CH}{-}CH_2{-}CHCl{-}CH{=}CH_2} \quad \text{(I),}$$



$$\mathrm{CH_3{-}CH{=}CH{-}\underset{\displaystyle CH_3}{CH}{-}\underset{\displaystyle CH_2Cl}{CH}{-}CH{=}CH_2} \quad \text{(II),}$$



$$\mathrm{CH_3{-}CH{=}CH{-}\underset{\displaystyle CH_3}{CH}{-}CH_2{-}CH{=}CH{-}CH_2Cl} \quad \text{(III)}$$

This small number of the expected addition products made the investigation of the reaction of 2-chloro-3--pentene with divinyl of particular interest because its results should be both convincing and simple in character while at the same time it should be possible to extend the conclusions from these results to more complex cases.

We investigated the reaction of 2-chloro-3-pentene with divinyl in the presence of stannic chloride in methylene chloride. The mixtures of telomers obtained were easily separated by distillation under vacuum into substances with the formula $C_9H_{15}Cl$ and the higher telomers. The relative yield of the former depended on the extent of the conversion: with extensive telomerization of the order of 55, 85 and 100% it was 80, 75 and 65%, respectively. In this reaction, as in the reaction of 2-chloro-3-pentene with isoprene [1], the yield of simple addition products was, therefore, considerable even in the most unfavorable instance (100% conversion).

When fractionally distilled, the substances with the formula $C_9H_{15}Cl$ are readily separated into two fractions of 58-60° and 69-72° (10 mm). The first of these was practically one compound. Its spontaneous separation into a number of members as a result of distillation gave fractions with identical constants; the second was undoubtedly a mixture of at least two substances.

The structure of the low-boiling substance was proven in the following manner.

1. The substance hardly took part in the Sommelet reaction [2, 3] and formula (III) is, therefore, excluded from it.

2. On ozonization it gave formic and acetic acid. Other ozonization products were not isolated. These data, also, exclude formula (III).

3. When the substance was reduced by Pd/ $CaCO_3$, 4-methyloctane was obtained. The identity of the latter

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* Diene Addition. LXIX. The reaction of dienes with haloid derivatives. IV.

with known 4-methyloctane was established from the combined dispersion spectrum. The 969, 988 and 1354 $cm^{-1}$ frequencies, characteristic of 3,4-dimethylheptane [4], which could be formed as a result of the hydrogenation of the substance with formula (II) were not found. Formula (II) was, therefore, also excluded.

4. In the infrared spectrum of the substance there were intense frequencies characteristic of a vinyl group (6060, 1629, 992 and 918 $cm^{-1}$).

All these data made it possible to attribute formula (I) to the low-boiling substance.*

It should be noted that as a result of the partial hydrogenation of 3-chloro-5-methyl-1,6-octadiene (I) rearrangement takes place and instead of the expected 5-methyl-1,6-octadiene, its isomer, 5-methyl-2,6-octadiene, is obtained mixed with the products of further hydrogenation. When ozonized it gives acetic and methylsuccinic acid. In the infrared spectrum there are frequencies of the $-CH{=}CH$ group (1660 and 957 $cm^{-1}$) while frequencies of the vinyl group are absent.

The structure of the main part of the high-boiling fraction was established by the same methods.

1. Approximately 65% of the fraction took part in the Sommelet reaction and it, therefore, contained not less than 65% of the primary chloride (III). This led to the formation of the corresponding diene aldehyde, 5-methyl-2,6-octadiene aldehyde, with a yield of about 60% of the reacted product. The structure of the aldehyde raises no doubts because it can only be obtained from substance (III). In the infrared spectrum of the aldehyde, in accordance with the proposed structure, the frequency of 1670 corresponds to a carbonyl group, 1640 to the double bonds and 970 $cm^{-1}$ to the $-CH{=}CH-$ group.

2. As a result of the splitting up of the high-boiling fraction by ozone, acetic, chloroacetic and methylsuccinic acids were obtained, which again corresponds to formula (III).

3. On hydrogenation of the investigated fraction by $Pd/CaCO_3$ 4-methyloctane was obtained. The identity of the hydrocarbon with known 4-methyloctane was established from the combined dispersion spectrum. As in the first instance the frequencies of 3,4-dimethylheptane were not found.

5. In the infrared spectrum of this fraction there are intense frequencies of 1660 and 968 $cm^{-1}$ corresponding to the $-CH{=}CH-$ group of the isomer (III).

All these data leave no doubt that the high-boiling fraction of the initial telomerization products consists primarily of a substance with formula (III).

In order to establish the structure of the products in the second fraction which did not take part in the Sommelet reaction we subjected the residue obtained after the separation of the aldehyde to hydrogenation by $Pd/CaCO_3$. As a result a low yield of a hydrocarbon similar in properties to methylethylcyclohexane was obtained. The latter can be formed by the hydrogenation of the cyclic chloride (IV) which is the isomerization (cyclization) product of substance (III).

The residue after the Sommelet reaction evidently contains not only this cyclic chloride but also some other substances with a carbon atom of low mobility. In the infrared spectrum of this residue, in addition to the 1680 and 972 $cm^{-1}$ frequencies which can be attributed to the cyclic chloride there are other frequencies, for example 912 and 923 $cm^{-1}$, which are obviously due to the presence of admixtures. The residue does not contain vinyl groups because the 6060 $cm^{-1}$ frequency was not found in the spectrum. The isomer (II) was, therefore, not present in the residue.

It was, therefore, established that as a result of the addition of 2-chloro-3-pentene to divinyl the isomeric chlorides (I) and (III) are formed in approximately equal amounts. Both chlorides form about 80% of the whole amount of the addition products in a ratio of 1 : 1. The other 20% consists of the cyclic chloride (IV) and admixtures of unknown structure. The isomer (II) was not found in the telomerization products.

It is interesting to note that under the same conditions isoprene gives 90% of the 1,4 product with 2-chloro-3-pentene [1].

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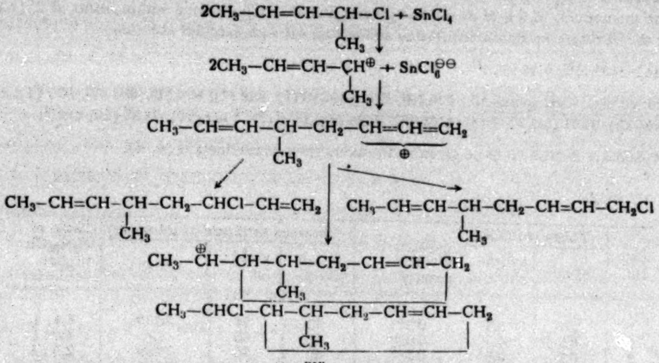
* It must be noted that as a result of telomerization with an extensive conversion of about 100% a product containing far less of substance (I) is sometimes obtained.

The higher fractions of the telomerization products were not investigated in detail. Only the infrared spectrum of the 125-135° (5 mm) fraction was investigated, frequencies being found which corresponded both to the vinyl group (6060, 980 and 920 $cm^{-1}$) and the $-CH=CH-$ group (970 $cm^{-1}$). These data indicate that further telomerization also takes place with the formation of the 1,2- and 1,4- products.

The entire process of the formation of the chlorides $C_9H_{15}Cl$ from 2-chloro-3-pentene and divinyl can be represented in the form of the following system:



(IV)

EXPERIMENTAL

Technical divinyl ($C_4H_6$ content 90%) was used for the investigation. 2-Chloro-3-pentene was obtained by the hydrochlorination of piperidine [1].

Telomerization was carried out in the apparatus previously described [5]. A 20% solution of stannic chloride in methylene chloride (2-4 ml per mole of divinyl) was added to the stirred and cooled mixture of divinyl and an equivalent amount of 2-chloro-3-pentene in 30% (by volume) methylene chloride. When a specific increase in the specific gravity was attained, telomerization was interrupted by the addition of 1.5 ml of diethylamine and the reaction mixture was distilled under vacuum. 20-60 min were required for one experiment.

The results of some of the experiments are given in Table 1. The fraction with a b.p. of 58-80° (10 mm) was used for the chlorides $C_9H_{15}Cl$.

The results of the double distillation of the chlorides $C_9H_{15}Cl$, obtained in Experiment 4, in a Widmer column (25 cm) are given below: 1st fraction up to 58°, 1.0 g; 2nd, 58-62°, 23 g; 3rd, 62-69°, 3.5 g; 4th, 69-72°, 37.2 g; 5th, 72-80°, 2.5 g; 6th, 80-100°, 5 g; 7th, 100-120°, 5.7 g; residue 34 g.

Investigation of the 2nd fraction. On repeated distillation the 2nd fraction passes over almost entirely within a temperature range of 1°.

B.p. 58-59° (10 mm), $d^{20}_4$ 0.8977, $n^{20}D$ 1.4575, $MR_D$ 48.18; calc. 47.70.

Found %: C 68.18; H 9.59; Cl 21.94. $C_9H_{15}Cl$. Calculated %: C 68.12; H 9.53; Cl 22.35.

a) When the substance was treated with urotropine according to the Sommelet-Leets reaction [3] about 1.5% of the former entered into the reaction over a period of 1 day.

b) 5.32 g of the substance in 60 ml of ethyl chloride was ozonized until the absorption of ozone had completely ceased. The ozonides were decomposed with 7-8% hydrogen peroxide. An aqueous solution of the fission products of the ozonides was extracted with ether. After the ether had been distilled the residue was fractionated under vacuum. A low-boiling distillate was obtained in which formic and acetic acid were detected (the former being detected by the reduction of an ammoniacal solution of silver oxide). From the acetic acid acetanilide was obtained with an m.p. of 111°. A mixed sample with known acetanilide had an m.p. of 111-112°.

We tried to isolate methylglutaric acid from the aqueous part of the ozonization products but were unsuccessful.

c) 9.38 g of the substance was reduced in a solution of methyl alcohol in the presence of 40 g of Pd/ $CaCO_3$ with a content of 0.01 g per g of catalyst. 3638 ml of hydrogen (752.5 mm, 19°) was absorbed, which corresponds to 83% of the theoretical. 6.9 g of an oil, the greater part of which distilled within limits of 2° (4.5 g), was obtained from the distillate by steam distillation and salting out with calcium chloride.

B.p. 141-143°, $d^{20}_4$ 0.7249, $n^{20}D$ 1.4082.

Combined dispersion spectrum. 732 (0), 776 (0), 818 (1), 832 (1), 874 (1), 894 (7), 937 (1), 1033 (2), 1051 (2), 1080 (5), 1101 (5), 1147 (6), 1192 (7), 1298 (8), 1340 (3), 1437 (10), 1455 (10) $cm^{-1}$.

These data are similar to those given in literature for 4-methyloctane [4, 6].

TABLE

| Expt. No. | Taken (in mole) |  | Increase in specific gravity | Obtained (mixture of telomers) |  |  | Ratio of $C_9H_{15}Cl$: higher telomers |
|---|---|---|---|---|---|---|---|
|  | divinyl | hydrochloride |  | weight (in g) | yield (as %) | % Cl |  |
| 1 | 0.5 | 0.5 | 0.053 | 43 | 54 | 20.72 | 4.3 : 1 |
| 2 | 0.5 | 0.5 | 0.058 | 48 | 60 | — | 4.0 : 1 |
| 3 | 0.5 | 0.5 | 0.087 | 60 | 76 | 19.89<br>20.01 | 2.5 : 1 |
| 4 | 1.0 | 1.0 | — | 120 | 76 | — | 2.2 : 1 |
| 5 | 0.5 | 0.5 | 0.102 | 80 | 100 | — | 2.0 : 1 |

1.93 g of the chlorine ion (92% of that contained in the initial substance was found in the residue).

d) 15.7 g of the substance in 100 ml of methanol was hydrogenated with Pd/ $CaCO_3$ (25 g) until 1.1 mole of hydrogen (2520 ml $H_2$ at 767.5 mm and 19°) had been absorbed. The reaction products were separated by the method previously described. 2.624 g of the chlorine ion was found in the solution, corresponding to 74.8% of that contained in the sample. 6.5 g of hydrocarbon and 3 g of residue were obtained.

B.p. 59-60° (50 mm, 138-139° (753 mm), $d^{20}_4$ 0.7427, $n^{20}D$ 1.4280.

Found %: C 86.27, 86.35; H 13.64, 13.78. $C_9H_{16}$. Calculated %: C 87.02; H 12.98. $C_9H_{18}$. Calculated %: C 85.63; H 14.38.

22.4 g of bromine was used for the bromination of 12.4 g of the hydrocarbon (70% of the calculated amount for two double bonds).

Acetic and methylsuccinic acid were found in the decomposition products of the ozonides of the hydrocarbon (3.8 g). The m.p. of the methylsuccinic acid was 109° (from benzene).

Found %: C 45.79, 45.82; H 6.00, 5.92. $C_5H_8O_4$. Calculated %: C 45.46; H 6.06.

e) The infrared spectrum of the substance is shown in Fig. 1. The main frequencies are:

696 s, 763 s, 847 m, 894 m, 918 s, 971 s, 992 s, 1031 m, 1085 m, 1244 s, 1374 s, 1449 s, 1629 m, $cm^{-1}$.

Investigation of the 4th fraction. The following data were obtained for this fraction:

B.p. 69-72° (10 mm), $d^{20}_4$ 0.9212, $n^{20}D$ 1.4698, $MR_D$ 48.03; calc. 47.70.

Found %: C 67.98, 67.92; H 9.70, 9.49; Cl 22.19, 22.06. $C_9H_{15}Cl$. Calculated %: C 68.12; H 9.53; Cl 22.35.

a) About 65% of the primary chloride was found in the fraction by the Sommelet-Leets method (Reaction time 2 days).

When 10 g of the fraction was heated with 10 g of urotropine in 45 ml of methylene chloride for 19 hours followed by treatment of the mixture twice with water,an aqueous layer and a layer of methylene chloride were obtained. The aqueous layer was distilled with formalin. An aldehyde, 5-methyl-2,6-octadiene aldehyde, was extracted from the distillate. The yield was 4 g (46% of the chloride taken and 66% of that which reacted). It had an odor of forest bugs.*

B. p. 94-95° (20 mm), $d^{20}_4$ 0.8659, $n^{20}D$ 1.4710, $MR_D$ 44.61, calc. 42.84.

Found %: C 78.14, 78.04; H 10.16, 10.39. $C_9H_{14}O$. Calculated %: C 78.21; H 10.22.

Infrared spectrum: 790 m, 844 vw, 888 w, 918 w, 973 vs, 1013 m, 1103 s, 1115 s, 1146 s, 1183 m, 1345 w, 1379 m, 1460 s, 1640 vs, 1670 vs, 2730 s, 2804 m, 2852 m, 2864 m, 2920 s, 2956 s, 3016 m, 3369 w,cm$^{-1}$.

Semicarbazone. M.p. 149.5-150.5° (from aqueous alcohol).

Found %: N 21.69, 21.77. $C_{10}H_{17}ON_3$. Calculated %: N 21.53.

2,4-Dinitrophenylhydrazone. M.p. 120.5-121°. Orange crystals (from alcohol).

Found %: N 17.48, 17.40. $C_{15}H_{18}O_4N_4$. Calculated %: N 17.60.

About 3.5 g of residue was obtained after the methylene chloride had been distilled. When it was distilled under vacuum 2 g of a main fraction was obtained.

B.p. 69-70° (10 mm), $d^{20}_4$ 0.9595, $n^{20}D$ 1.4732.

Found %: C 68.81, 69.00; H 9.59, 9.75. $C_9H_{15}Cl$. Calculated %: C 68.12; H 9.53.

When 152 g of the 66-79° (10 mm) fraction with a primary chloride content of 65% was treated with urotropine by the Sommelet method 48 g (32%) of unreacted chlorides was obtained. When the latter were distilled under vacuum (10 mm) the following fractions were obtained: 1st, 59-61°, 12 g, (1,2 product), 2nd, 61-65°, 2 g; 3rd, 65-70°, 3g; 4th, 70-78°, 23 g; residue 4.7 g.

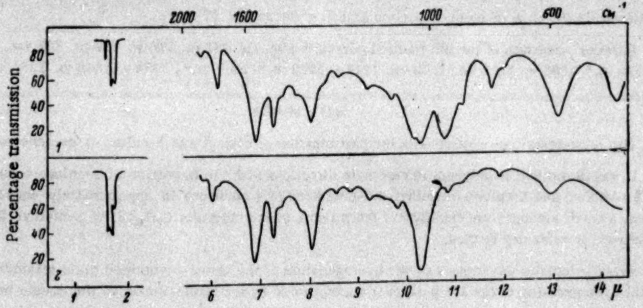


Fig. 1. Infrared transmission spectra (prisms of NaCl and glass, layer thickness 1 mm). 1) 58-59° (10 mm) fraction; 2) 69-72° (10 mm) fraction.

20 g of the 4th fraction was treated with urotropine again. The residue (16.5 g) was again distilled. The following fractions were obtained: 1st, 70-72°, 1.3 g; 2nd, 72-73°, 1.3 g; 3rd, 73-75°, 8 g; 4th, 75-78°, 4.2 g.

The following data were obtained from the 3rd fraction: $d^{20}_4$ 0.9749, $n^{20}D$ 1.4782.

Found %: C 69.66, 69.56; H 9.82, 9.91. $C_9H_{15}Cl$. Calculated %: C 68.12; H 9.53. Number of double bonds by Kaufmann's method 1.07.

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*As in original — Publisher's note.

The values found for the 3rd fraction were: $d^{20}_4$ 0.9787, $n^{20}D$ 1.4812.

Found %: C 69.54; H 9.78. $C_9H_{15}Cl$. Calculated %: C 68.12; H 9.53.

A mixture of proportional amounts of the 3rd and 4th fractions (7.25 g) was hydrogenated with Pd/ $CaCO_3$ until the absorption of hydrogen ceased. 1307 ml of hydrogen (765.5 mm, 18°) was absorbed, corresponding to 58% on the assumption of one double bond and a chlorine atom. The hydrogenation products were steam-distilled. 0.532 g of chlorine ion was found, representing about 33% of that contained in the sample.

An oil (4.4 g) was obtained from the distillate; when it was distilled a hydrocarbon (2 g) was isolated.

B.p. 152-157°, $d^{20}_4$ 0.8014, $n^{20}D$ 1.4380.

Found %: C 85.17, 85.22; H 14.35, 14.42. $C_9H_{18}$. Calculated %: C 85.63; H 14.37.

These data are similar to those given in literature for 1-methyl-2-ethylcyclohexane [6].

b) When 9.65 g of the fraction was hydrogenated 3469 ml of hydrogen (752 mm, 20.5°) was absorbed, corresponding to 82% of the theoretical amount. 5.2 g of hydrocarbon was obtained (52% calculated on the initial product, 63% on the absorbed hydrogen).

B.p. 140-142°, $d^{20}_4$ 0.7247, $n^{20}D$ 1.4088.

Combined dispersion spectrum: 731 (0), 777 (0), 825 (1), 872 (1), 897 (7), 936 (2), 1033 (2), 1051 (?), 1090 (5), 1146 (6), 1192 (7), 1241 (1), 1297 (8), 1338 (3), 1373 (3), 1438, 1455 (10) $cm^{-1}$.

1.79 g of chlorine ion was found in the solution (82% of that contained in the sample).

c) A mixture of acids was extracted with ether from the ozonization products of 5.5 g of the fraction in 60 ml of ethyl chloride (followed by decomposition with 7-8% hydrogen peroxide). When the mixture was distilled under vacuum the following were obtained: acetic acid (acetanilide m.p. 110-112°, m.p. of a mixed melt 111-112°), chloroacetic acid (m.p. 61-62°, m.p. of a mixed melt 61-62°) and a residue. The latter was placed on a porous plate. The separated crystals of methylsuccinic acid were removed and recrystallized from benzene after the substance had an m.p. of 108.5-110°.

Found %: C 45.55, 45.42; H 5.98, 5.95. $C_5H_8O_4$. Calculated %: C 45.46; H 6.06.

In literature the m.p. of methyl succinic acid is given as 112° [7].

d) Infrared spectrum of the 4th fraction (Given in Fig. 1): 681 m, 726 w, 769 m, 837 vw, 897 w, 922 w, 969 vs, 1015 m,* 1080 w, 1131 vw, 1172 vw, 1244 s, 1292 m,* 1350 m.*, 1374 s, 1449 vs, 1630 vw, 1656 m $cm^{-1}$

## SUMMARY

1. The telomerization reaction with the participation of divinyl and 2-chloro-3-pentene was investigated.

2. It was shown that it proceeds in two main directions with the formation of 3-chloro-5-methyl-1,6-octadiene (1,2 addition) and 1-chloro-5-methyl-2,6-octadiene (1,4 addition) in approximately equal quantities. In addition, a small amount (less than 20% of the mixture of the chlorides $C_9H_{15}Cl$) of 1-methyl-2-chloroethyl-4-cyclohexene is evidently formed.

3. 4-Methyloctane was formed by the hydrogenation of the above-mentioned main telomerization products. The partial hydrogenation of the 1,2 product is accompanied by the displacement of the double bond and gives an unsaturated compound corresponding in structure to the 1,4 product.

4. An aldehyde, 5-methyl-2,6-heptadiene aldehyde, was obtained from 1-chloro-5-methyl-2,6-octadiene by the Sommelet reaction. Its crystalline derivatives, the semicarbazone and the 2,4-dinitrophenylhydrazone, were characterized.

5. On the basis of a comparison of the data obtained on the order of addition of 2-chloro-3-pentene to divinyl with similar data previously obtained for isoprene the conclusion was drawn that the structure of the diene hydrocarbon has an important influence on the order of addition of the haloid derivatives.

## LITERATURE CITED

[1] A. A. Petrov, N. A. Razumova and M. L. Genusov, J. Gen. Chem. 28, 1128 (1958).*

[2] Org. Reactions. 8, 263 (1957).**

[3] K. V. Leets, A. I. Piliavskaia and M. I. Korovkina, J. Gen. Chem. 27, 2969 (1957).*

[4] G. S. Landsberg, P. A. Bazhulin and M. M. Sushchinskii, Main Parameters of the Combined Dispersion Spectra of Hydrocarbons, Acad. Sci. USSR Press (1956).**

[5] A. A. Petrov, Kh. V. Bal'ian, Iu. I. Kheruze, E. Iu. Shvarts and L. L. Cherenkova, J. Gen. Chem. 28, 1435 (1958).*

[6] R. D. Obolentsev, The Physical Constants of Hydrocarbons, Gostoptekhizdat (1953).**

[7] Dictionary of Organic Compounds (1949).**

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**In Russian.

# INVESTIGATIONS IN THE FIELD OF CONJUGATED SYSTEMS

## XCI. THE ADDITION OF 1-CHLORO-3-METHYL-2-BUTENE TO DIVINYL*

A.A.Petrov and N.A. Razumova

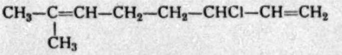
The reaction of divinyl with 1-chloro-3-methyl-2-butene is a more complex instance of a telomerization reaction than the previously described reaction of divinyl with 2-chloro-3-pentene [1] because of the tendency of this haloid derivative to allyl rearrangement. As a result of the addition of 1-chloro-3-methyl-2-butene to divinyl the formation of 6 open-chained substances of the composition $C_9H_{15}Cl$ and 2 cyclic compounds could be expected.

The mixture of telomers actually obtained was readily separated by vacuum distillation into the chlorides $C_9H_{15}Cl$ and the higher telomers. The ratio between these products depended markedly on the extent of conversion. With conversion of the order of 50% the yield of the chlorides $C_9H_{15}Cl$ was 35% but with about 100% conversion the yield fell to 20%. (The remainder consisted of higher telomers and, possibly, dimers of the chloride).

In this instance, therefore, the higher telomers are formed in approximately the same amounts as in the reaction of 1-chloro-3-methyl-2-butene with isoprene [2] and in considerably larger amounts than in the reaction of 2-chloro-3-pentene with divinyl [1] and isoprene [3].

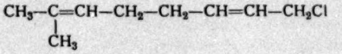
In this investigation we characterized the lower fractions of the telomerization products with the formula $C_9H_{15}Cl$ which distilled under vacuum at 10 mm up to 80°. Only a mixture of products with the composition $C_5H_7-(C_4H_6)_2-Cl$, distilling under vacuum at 125-129° (2 mm) was isolated from the higher fractions.

The most probable initial telomerization products of 1-chloro-3-methyl-2-butene and divinyl were the three following compounds:



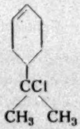
$$\underset{\displaystyle CH_3}{CH_3-\overset{}{C}}=CH-CH_2-CH_2-CHCl-CH=CH_2$$

(I)



$$\underset{\displaystyle CH_3}{CH_3-\overset{}{C}}=CH-CH_2-CH_2-CH=CH-CH_2Cl$$

(II)



(III)

Conclusions regarding the composition of this part of the telomers were drawn on the basis of the following data.

1. The mixture of the chlorides $C_9H_{15}Cl$ took part only 7-10% in the Sommelet reaction after continued treatment with urotropine. The aldehyde formed was isolated in the form of the 2, 4-dinitrophenylhydrazone. The isomer (II) is, therefore, contained in the investigated mixture, but only a small amount is present.

2. The following were detected in the fission products obtained from a mixture of ozonides: formaldehyde (determined in the form of the dinaphtholmethane), acetone (isolated in the form of the 2, 4-dinitrophenylhydrazone), chloroacetic, succinic and α-chloroglutaric acids. These data indicate that the mixture consists primarily

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* Diene Compounds. LXX. The reaction of dienes with haloid derivatives V.

of the chlorides (I) and (II).

3. As a result of the exhaustive hydrogenation of the mixture by $Pd/CaCO_3$, 2-methyloctane, with constants similar to those given in literature [4], was obtained. The combined dispersion spectrum of the hydrocarbon also hardly differed from the value given for this substance in literature [5]. The frequencies characteristic for 2,5-dimethylheptane (768 and 907 $cm^{-1}$) and 3,3,4-trimethylhexane (532, 704, 1211 $cm^{-1}$) were absent in this spectrum. (The first of these hydrocarbons can be obtained by the hydrogenation of the product of the addition of 1-chloro-3-methyl-2-butene to divinyl in a manner contrary to Markownikoff's rule, the second can be obtained by the hydrogenation of the product of the addition of dimethylvinylchloromethane in the same order, i.e., the allyl isomer of 1-chloro-3-methyl-2-butene).

In addition to the frequencies of 2-methyloctane the spectrum contains, although very weakly expressed, the most intense of the characteristic frequencies of 3,3-dimethylheptane (724 $cm^{-1}$) and also the weak frequency 1263 $cm^{-1}$, clearly expressed in the spectrum of isopropylcyclohexane and absent in the spectra of all the other expected open-chained hydrocarbons. 3,3-Dimethylheptane can be formed by the hydrogenation of the addition product of divinyl and dimethylvinylchloromethane; isopropylcyclohexane – by the hydrogenation of substance (III).

The investigation of the hydrogenation products of the telomer makes it possible, therefore, to confirm that it consists primarily of substances (I) and (III).

It must be noted that as a result of the partial hydrogenation of a mixture of the chlorides, $C_9H_{15}Cl$ a diene hydrocarbon without a vinyl group is obtained. In the infrared spectrum of this hydrocarbon there are bands of the $-CH=CH-$ group at 960 and 1660 $cm^{-1}$ while the bands characteristic of the vinyl group are absent. A similar phenomenon also occurs in the hydrogenation of the addition products of divinyl and 2-chloro-3-pentene [1].

4. The infrared spectrum of the mixture of the chlorides $C_9H_{15}Cl$ also indicated that this is principally a case of a 1,2-product (I). In the spectrum there were intense bands characteristic of the vinyl group (6060, 1640, 920 and 980 $cm^{-1}$). The band of the $-CH=CH-$group which is included in the isomer (II) (960 $cm^{-1}$) was far more weakly expressed (Fig. 1, curve I).

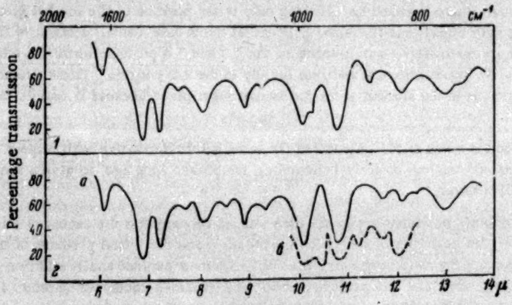
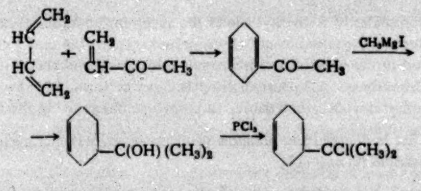


Fig. 1. The infrared transmission spectra.
1) Telomer with the composition $C_9H_{15}Cl$; 2a) second fraction of the telomer; 2b) fourth fraction of the telomer.

By various methods it was, therefore, established that the addition of 1-chloro-3-methyl-2-butene to divinyl takes place primarily in the 1,2 position according to Markownikoff's rule and is accompanied by hardly any allyl rearrangement.

It was natural to make attempts to isolate the 1,2 product in the pure form by fractional distillation but this was found to be a difficult task. When fractionated the mixture of chlorides divides up into two parts with boiling ranges of 62-65 and 73-76° (10 mm), the first fraction being the main one. The distillation character does not justify the assumption that either of these fractions is a pure substance. The 62-65° (10 mm) fraction contains a total of about 3% primary chloride. Intense bands of the vinyl group are found in its spectrum but there are no bands of the $-CH{=}CH-$ group. The 73-76° (10 mm) fraction contains about 40% primary chloride (II). In the infrared frequency of this fraction there is an intensefrequency of the $-CH{=}CH-$ group (960 $cm^{-1}$), but, as formerly, the frequencies of the vinyl group are also strongly represented. The impression is created that some other product containing a vinyl group is present in the mixture in addition to substance (I).

As already mentioned, judging from the combined dispersion spectrum of the hydrogenation products the mixture of telomers contains the cyclic chloride (III). We achieved its synthesis according to the system



The constants of the synthesized substance are markedly different from the constants of all the parts of the telomer $C_9H_{15}Cl$. The chloride (III) has a far higher specific gravity and refractive index. Its content in the telomer cannot, therefore, be very great. As a result of hydrogenation with Pd/$CaCO_3$ it gives isopropylcyclohexane with constants similar to those given in literature.

The structure of the telomerization products with the formula $C_5H_7-(C_4H_6)_2-Cl$ was only determined by the ozonization method. Formaldehyde, acetone, chloroacetic and succinic acid were found in the ozonization product. These data indicated that the higher telomers are a mixture of the 1,2- and 1,4- products.

As a result of this investigation it was, therefore, established that the order of addition and the extent of telomerization (under similar conditions) are determined by the structure of the diene hydrocarbon and the haloid derviative. When the two isomeric chlorides, differing only in the position of the methyl group with respect to the double bond, react with divinyl one (2-chloro-3-pentene) forms only a small amount of the higher telomers and gives a mixture of approximately equal amounts of the 1,2 and 1,4 products while the other (1-chloro-3-methyl-2-butene) gives primarily higher telomers and adds mainly in the 1,2 position. These two characteristics are possibly connected and the reduction in the amount of the 1,4 isomer takes place because it readily takes part in further conversions.

When a comparison is made of the behavior of the same haloid derivative with respect to different diene hydrocarbons the tendency of homologs of divinyl (isoprene), established long ago, to give a large amount of the 1,4 product than divinyl [6] is shown.

In one of the previously published papers the idea was put forward that the extent of telomerization is determined by the ratio of the activities of the initial hydrocarbon and the initial products of its addition to divinyl. In the light of these opinions the ratio of the activities of 2-chloro-3-pentene andits addition products with divinyl must be of much greater interest than the analogous ratio for 1-chloro-3-methyl-2-butene. It will only be possible to give a definite answer to this problem after investigating the rate of the exchange conversions with the participation of all these haloid derivatives and also their dipole moments.

## EXPERIMENTAL

The reaction of 1-chloro-3-methyl-2-butene with divinyl. Technical divinyl ($C_4H_6$ content 90%) was used for the investigation. 1-chloro-3-methyl-2-butene was obtained by the hydrochlorination of isoprene [2]. Many experiments on telomerization with varying degrees of conversion were carried out with these products. The data of two of these experiments are given below.

a) 1.5 ml of a 10% solution of stannic chloride in methylene chloride was added to a stirred and cooled mixture of 26 g of divinyl, 50 g of 1-chloro-3-methyl-2-butene and 37 g of methylene chloride. The temperature was kept at about 8-10°. Stirring was continued for 6 hours, measures being employed to recover the evaporating divinyl. Telomerization was then interrupted by the addition of 1.5 ml of diethylamine and the mixture was distilled under vacuum. The methylene chloride and the unreacted 1-chloro-3-methyl-2-butene were distilled under low vacuum (100 mm) and the reaction products at 10 mm. A total of 69 g of telomer was obtained. The approximate extent of telomerization was 85%. 23 g of the substance distilled off below 100° (10 mm). The residue was 45 g.

b) Under the same conditions 36 g of the telomer was obtained by stirring for 2 hours. On distillation 15 g of the chloride $C_9H_{15}Cl$ and 21 g of residue were obtained. The mixture of chlorides $C_9H_{15}Cl$ had a b.p. of 60-80°, $d^{20}_4$ 0.92 and $n^{20}D$ of about 1.4650. Its chlorine content was close to the theoretical, the amount of saponifiable chlorine being hardly different from the total chlorine content. Here are the analytical data of one of the samples.

Found %: Cl 22.32, 22.07. $C_9H_{15}Cl$. Calculated %: Cl 22.53.

This mixture of chlorides was treated with urotropine by the Sommelet method ozonized and hydrogenated.

a) 7-10% of 1-chloro-3-methyl-2-butene was found in it by the Sommelet-Leets method [7]. When 21 g of the mixture of chlorides was heated with 20 g of urotropine in 50 ml of methylene chloride for 4 hours followed by treatment of the mixture twice with water (75 ml each time), an aqueous solution and a residue dissolved in methylene chloride were obtained. An aldehyde which was treated, without purifying, with a solution of 2,4-dinitrophenylhydrazone was extracted from the distillate by ether. 2.8 g of the 2,4-dinitrophenylhydrazone of 7--methyl-2,6-octadiene aldehyde was obtained, corresponding to a 7.5% aldehyde content in the investigated product.

M.p. 95-96° (from alcohol). Orange-red needles.

Found %: N 17.47. $C_{15}H_{18}O_4N_4$. Calculated %: N 17.60.

After the methylene chloride had been distilled a residue (17 g) was obtained, the greater part of which distilled at about 48° (3 mm) and had $d^{20}_4$ 0.9248 and $n^{20}D$ 1.4638.

4.85 g of the residue was subjected to exhaustive hydrogenation on palladium catalyst (Pd/$CaCO_3$ – 9 g, with a content of about 0.01 g of Pd per g of $CaCO_3$) in methyl alcohol (60 ml). The distillate was diluted with a saturated solution of $CaCl_2$. When the oil which separated out was distilled with a small Widmer fractionating column the following fractions were obtained: 1st, 142-145°, 1.4 g ($n^{20}D$ 1.4080); 2nd, 145-150°, 0.5 g; 3rd, 150-170°, 0.2 g; 4th, above 170°, 0.8 g.

b) 3.1 g of a mixture of the chlorides was treated with ozone in ethyl chloride until absorption ceased. After the evaporation of the solvents the ozonides were decomposed with a solution of hydrogen peroxide. $^1/_5$ of the aqueous solution of the ozonide decomposition products was distilled off. When the distillate was treated with 2,4-dinitrophenylhydrazine, the 2,4-dinitrophenylhydrazone of acetone with an m.p. of 125-126° was precipitated. A mixed melt with the known compound melted at the same temperature.

The acids were extracted from the aqueous solution with ether in an extractor equipped with a stirrer. After the ether had been removed chloroacetic acid (which crystallized in the condenser) was distilled under vacuum from the residue. The m.p. was 61-62° (from petroleum ether). A mixed melt melted at the same temperature.

The partially crystallized residue was placed on a porous plate. The purified crystalline product had an m.p. of 184-185° (from benzene). A mixed melt with known succinic acid had the same melting point.

In order to reduce the α-hydroxyglutaric acid the aqueous solution remaining after the extraction of the chloroacetic and succinic acid was heated with hydriodic acid and was then extracted again with ether. Glutaric acid was isolated from the ethereal solution. The m.p. was 96-97° (from water). A mixed sample had the same melting point.

To detect formaldehyde 0.5 g of the chloride was ozonized, the ozonide being decomposed with a solution of potassium iodide. The excess iodine was back-titrated with hyposulfite and the formaldehyde was precipitated with a solution of β-naphthol. A copious precipitate of dinaphtholmethane with an m.p. of 186° [8] was obtained.

c) 5.4 g of the mixture of chlorides was subjected to exhaustive hydrogenation (catalyst – Pd/$CaCO_3$). 1990 ml of $H_2$ (765 mm, 19°) was absorbed, corresponding to 73% of the theoretical amount (allowing for 2 double bonds and 1 atom of halogen). 0.8947 g of chlorine ion was found in the solution, 74.2% of that contained in the sample.

The reaction products were steam-distilled and were salted out from the distillate with a solution of $CaCl_2$. The oil obtained was distilled with a small Widmer fractionating column. During fractionation it separated into a hydrocarbon with a b.p. of 141-143°, $d^{20}_4$ 0.7235, $n^{20}D$ 1.4075 (2 g) and higher-boiling products containing chlorine.

The combined dispersion spectrum of the hydrocarbon was determined.

249 (2), 723 (?) 751 (?), 805 (3), 886 (1), 952 (2), 1056 (1), 1074 (1), 1092 (1), 1129 (4), 1167 (2), 1263 (1), 1300 (5), 1336 (2), 1378* (0), 1394 (1), 1438-1458 (8 b) $cm^{-1}$.

These data are close to those previously found for 2-methyloctane [5].

The chlorides $C_9H_{15}Cl$ were distilled in a Widmer column (25 cm) at 10 mm. As a result of the distillation of the products obtained in two experiments at a conversion of the order of 80% the following fractions were obtained: 1st, up to 62°, 2.5 g; 2nd, 64-66°, 16 g ($d^{20}_4$ 0.9244, $n^{20}D$ 1.4630); 3rd, 66-76°, 5.7 g; 4th, 76-77°, 4.5 g ($d^{20}_4$ 0.9262, $n^{20}D$ 1.4705); 5th, 77-80°, 3.5 g ($n^{20}D$ 1.4750), residue 3 g.

3.18, 3.26% of primary chloride was found in the 2nd fraction by the Sommelet-Leets method [7] (the reaction mixture was shaken for 116 hours). Its infrared spectrum is given in Fig. 1, curve 2a.

4.2 g of hydrocarbon and 5 g of residue were obtained from the partial hydrogenation of this fraction (13.5 g) with Pd/ $CaCO_3$ (1 mole of $H_2$ per mole of substance) until 2,074 ml of hydrogen (770 mm, 21°) had been absorbed. 1.77 g of chlorine ion (58.8% of that contained in the sample) was found in the solution.

The following constants were found for the hydrocarbon (2-methyl-2,6-octadiene with an admixture of the products of further hydrogenation): b.p. 142-144°, $d^{20}_4$ 0.7460, $n^{20}D$ 1.4250. Observations regarding its structure, in accordance with its infrared spectrum, were made on the product (including the admixture).

The residue (5 g) and the hydrocarbon were subjected to exhaustive hydrogenation. A hydrocarbon with a b.p. of 141-143°, $n^{20}D$ 1.4070, was obtained; these data are similar to those given in literature for 2-methyloctane [4].

Found %: C 84.38, 84.32; H 15.74, 15.77. $C_9H_{20}$. Calculated %: C 84.28; H 15.72.

45.4, 46.5% of the primary chloride was found in the 4th fraction. The infrared spectrum is given in Fig. 1, curve 2b. In the exhaustive hydrogenation of this fraction 64% of the theoretical amount of hydrogen was absorbed. 82.4% of the theoretical amount of chloride ion was found in the solution. The hydrocarbon obtained hardly differed, as regards its constants, from that formed by the hydrogenation of the 2nd fraction.

The higher-boiling chlorides were distilled under vacuum at 2 mm. The products boiling in the 115-150° range (10 g) were redistilled. As a result the following fractions were obtained: 1st, 117-125°, 1.5 g; 2nd, 125--129°, 5 g; residue 2 g.

For the 125-129° (2 mm) fraction the following constants were obtained: $d^{20}_4$ 0.9520, $n^{20}D$ 1.4855. $MR_D$ 65.66; calc. 65.70.

Found %: C 71.79, 71.65; H 9.62, 9.52; Cl 18.64, 18.46. $C_{13}H_{21}Cl$. Calculated %: C 73.41; H 9.86; Cl 16.23.

Acetone, chloroacetic and succinic acid, and formaldehyde were obtained by the ozonization of 2.9 g of this fraction.

Synthesis and properties of chloroisopropyl-3-cyclohexene. The corresponding carbinol, obtained by a previously described method [9], was treated with the calculated amount of phosphorus trichloride in a medium of absolute ether. The ethereal solution was shaken with powdered chalk and washed with water. After it had been dried over $CaCl_2$ the reaction product was distilled under vacuum.

B.p. 75-76° (10 mm), $d^{20}_4$ 0.9951, $n^{20}D$ 1.4828, $MR_D$ 45.52; calc. 44.96.

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* This frequency is probably excited by another line of mercury.

Found %: C 68.83, 68.73; H 9.71, 9.56; Cl 22.46, 22.50. $C_9H_{15}Cl$. Calculated %: C 68.13; H 9.46; Cl 22.32.

8.5 g of the substance was hydrogenated in the pesence of Pd/ $CaCO_3$ (18 g) in 120 ml of methyl alcohol. 1530 ml of $H_2$ (758 mm, 19°) was absorbed, corresponding to 58% of the theoretical (assuming 1 double bond and 1 atom of chlorine). The mixture was steam-distilled. 1.9 g of chlorine ion, 78.4% of that contained in the sample, was found in the residue. The distillate was diluted with a saturated solution of $CaCl_2$. The oil was dried over $CaCl_2$ and was distilled with a small Widmer fractionating column. 3 g of hydrocarbon with a b.p. of 154-156°, $d^{20}_4$ 0.8108, $n^{20}$D 1.4452 was obtained. These data are similar to those given in literature for isopropylcyclohexene [4].

Found %: C 85.96, 85.84; H 13.97, 14.02. $C_9H_{18}$. Calculated %: C 85.63; H 14.37.

## SUMMARY

1. The reaction of 1-chloro-3-methyl-2-butene with divinyl in the presence of stannic chloride was investigated.

2. It was shown that in comparison with the previously described reaction of 2-chloro-3-pentene with divinyl the yield of chlorides with the composition $C_9H_{15}Cl$ is much lower and depends primarily on the extent of the conversion.

3. It was established that 1-chloro-3-methyl-2-butene adds to divinyl principally in the 1,2 position whereas it adds to isoprene mainly in the 1,4 position.

4. 7-methyl-2,6-octadiene aldehyde was obtained from the 1,4 product by the Sommelet reaction.

5. On the basis of an investigation of the combined dispersion spectra of the hydrogenation products of the chlorides with the composition $C_9H_{15}Cl$ the conclusion was drawn that the reaction products did not contain appreciable amounts of isomers,formed as a result of the addition of a haloid derivative in a manner contrary to Markownikoff's rule, or addition products of the isomer of 1-chloro-3-methyl-2-butene, dimethylvinylchloromethane.

6. It was shown that as a result of the partial hydrogenation of the 1,2 product the double bond is displaced and the hydrogenation product, evidently 2-methyl-2,6-octadiene, does not contain a vinyl group.

7. The expected cyclic chloride, chloroisopropyl-3-cyclohexene, was obtained from the corresponding alcohol by the action of phosphorus trichloride. It was established that its content in the mixture of telomers is low.

## LITERATURE CITED

[1] A. A. Petrov, N. A. Razumova and M. L. Genusov, J. Gen. Chem. 28, 2132 (1958).*

[2] A. A. Petrov, Kh. V. Bal'ian, Iu. I. Kheruze, E. Iu. Shvarts and L. L. Cherenkova, J. Gen. Chem. 28, 1435 (1958).*

[3] A. A. Petrov, N. A. Razumova and M. L. Genusov, J. Gen. Chem. 28, 1128 (1958).*

[4] R. D. Obolentsev, The Physical Constants of Hydrocarbons, Gostoptekhizdat (1953).**

[5] G. S. Landsberg, P. A. Bazhulin, M. M. Sushchinskii, Principal Characteristics of the Combined Dispersion Spectra of Hydrocarbons, Acad. Sci. USSR Press (1956).**

[6] A. A. Petrov, Progr. Chem. 22, 905 (1953).

[7] K. V. Leets, A. I. Piliavskaia and M. I. Korovkina, J. Gen. Chem. 27, 2969 (1957).*

[8] Dict. Org. Compounds, Foreign Lit. Press. (1949).[Russian translation].

[9] A. A. Petrov, J. Gen. Chem. 11, 309 (1941).

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*Original Russian pagination. See C.B. translation.

**In Russian.

# THE CONDENSATION OF DIENE HYDROCARBONS WITH CINNAMALEDHYDE. THE SYNTHESIS OF HYDROAROMATIC ALCOHOLS, ACETATES AND HYDROCARBONS

N. P. Sopov and M. L. Kovner

In previous papers the problem was considered of the possibility of obtaining hydroaromatic alcohols and hydrocarbons on the basis of the condensation products of 1,3-diene hydrocarbons with $\alpha,\beta$-unsaturated carbonyl compounds, acids and their derivatives [1-6].

Continuing the investigations in the same direction we studied the condensation of divinyl, piperylene, isoprene, diisopropenyl, cyclopentadiene and cyclohexadiene with cinnamaldehyde. Secondary alcohols, their acetates and (by the pyrolysis of the latter) hydroaromatic hydrocarbons were synthesized from the aldehydes obtained.

In the literature there are data on the condensation of cinnamaldehyde with $\alpha,\gamma$- and $\beta,\gamma$-dimethylbutadiene and with 1-vinylnaphthalene and piperylene [7-10].

The constants, analytical data and yields of 2-phenyltetrahydrobenzaldehyde and its homologs are given in Table 1.

1,3-cyclopentadiene did not take part in condensation with cinnamaldehyde. In the case of 1,3-cyclohexadiene the yield of the addition product was lower than for acyclic dienes. This can probably be explained by the fact that the molecules which have endo "bridges" have a greater tendency to dissociate into the initial components. With the homologs of divinyl the yield of the addition products is much higher than in the case of divinyl.

Phenyltetrahydrobenzaldehydes are viscous yellowish liquids with hardly any odor. They are all insoluble in water but dissolve well in ether, alcohol and benzene. The p-nitrophenylhydrazones and 2,4-dinitrophenylhydrazones of all the aldehydes were prepared and recrystallized from aqueous alcohol. The melting points and the analytical data of the hydrazones are given in Table 2.

The secondary alcohols were obtained by the action of methylmagnesium iodide on 2-phenyltetrahydrobenzaldehyde and its homologs. The alcohols have a still higher viscosity than the corresponding aldehydes. They are yellowish liquids with a flower-like odor. They are soluble in ether, alcohol and benzene.

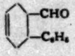
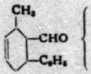
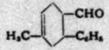
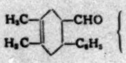
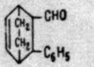
The alcohol obtained from 2-phenyltetrahydrobenzaldehyde was separated into crystalline and liquid products (in a ratio of 2 : 1). They were probably the cis and trans forms of the substance. The constants of the alcohols, the analytical data and the yield are given in Table 3.

The acetates of these alcohols are yellowish liquids with a lower viscosity than the initial alcohols. They have a flower-like odor. From Table 4 it is evident that the acetates boil approximately 4° higher than the initial alcohols and have almost the same specific gravities but have considerably smaller refractive indices.

We obtained the hydroaromatic hydrocarbons by the pyrolysis of the acetates. On the basis of previously established laws which showed that in the pyrolysis of acetates dehydration takes place in one direction we gave the substances obtained the formulae shown in Table 5 [11-13]. Hydroaromatic carbons of the type under consideration are readily dehydrated on platinized charcoal.

TABLE 1

Aldehydes

| Substance | Boiling point (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ |  | Found % |  | Calc. % |  | Yield (as %) on heating to |  |
|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  | found | calc. | C | H | C | H | 170—180° | 180—200° |
|  | 141—142°<br>(10) | 1.0642 | 1.5538 | 56.06 | 55.98 | 83.80, 83.65 | 7.85, 7.99 | 83.83 | 7.57 | 30 | 46 |
|  | 150—152<br>(11)<br>149—150 (10) | 1.0540<br>1.0510 | 1.5465 [10]<br>1.5458 | —<br>60.32 | —<br>60.59 | 84.07<br>83.82 | 8.42<br>8.33 | —<br>83.96 | —<br>8.05 | —<br>— | —<br>65 |
|  | 154—155<br>(10) | 1.0430 | 1.5468 | 60.88 | 60.59 | 83.91, 84.00 | 8.28, 8.13 | 83.96 | 8.05 | 44 | 65 |
|  | 164.5—166,<br>171—173 [8]<br>(3.5) | 1.0464<br>1.0400 | 1.5483<br>1.54843 | 65.14<br>65.29 | 65.21<br>65.21 | 84.44, 84.32<br>— | 8.72, 8.79<br>— | 84.07<br>— | 8.46<br>— | —<br>— | 68<br>— |
|  | 169—170<br>(10) | 1.1053 | 1.5740 | 63.38 | 63.01 | 84.81, 85.08 | 7.26, 7.36 | 84.87 | 7.59 | — | 22 |

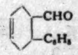
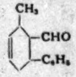
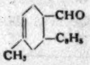
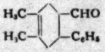
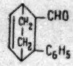
# EXPERIMENTAL

The condensation of dienes with cinnamaldehyde. Cinnamaldehyde with the following constants was used for this work: b.p. 130° (20 mm), $d^{20}_4$ 1.099, $n^{20}_D$ 1.6195 [14]. Technical (90%) divinyl and piperylene were used. Condensation was carried out in autoclaves in a solution of toluene in the presence of hydroquinone with heating at 180-220° for 10-12 hours.

1 mole of cinnamaldehyde and 1.5 mole of diene hydrocarbon were used for the condensation.

TABLE 2

Hydrazones and the Aldehydes

| Aldehydes | Melting point | | Found % N | Calculated % N |
|---|---|---|---|---|
| | of the p-nitrophenylhydrazones | of the 2,4-dinitrophenylhydrazones | | |
|  | 198—199° | — | 13.42 | 13.08 |
| | — | 181—182° | 15.44 | 15.30 |
|  | 149—150 | — | 12.30 | 12.53 |
| | — | 103.5—104.5 | 14.57 | 14.74 |
|  | 161—162 | — | 12.80 | 12.53 |
| | — | 129—130 | 15.08 | 14.74 |
|  | 169—170 | — | 11.95 | 12.03 |
| | — | 150—152 | 14.35 | 14.21 |
|  | 154—155 | — | 12.05 | 12.12 |
| | — | 148—149 | 14.21 | 14.28 |

Preparation of the secondary alcohols. A solution of 0.2 mole of hydroaromatic aldehyde in 50 ml of ether was added with mechanical stirring to a solution of the organomagnesium compound obtained from 0.2 g of magnesium and 0.22 mole of methyl iodide in 100 ml of absolute ether. After the mixture had been heated for 4 hours it was left to cool overnight. The organomagnesium complex was decomposed in the usual manner. The ethereal solution of the secondary alcohol was dried with calcined sodium sulfate and distilled.

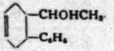
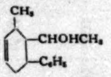
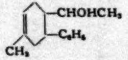
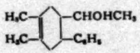
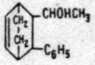
Preparation of the acetates. 1 drop of sulfuric acid was added to 0.1 mole of secondary alcohol and 0.15 mole of acetic anhydride. The mixture was heated on a water bath to 40-50° after which it was shaken and cooled from time to time with a jet of water to keep the temperature below 80-90°. The mixture was then diluted with water and the acetate was extracted with ether. The ethereal extract was washed with a solution of soda, then with water; it was dried over calcined sodium sulfate and distilled.

Pyrolysis of the acetates. The pyrolysis of the acetates was carried out at 430-450° in a quartz tube filled with fine quartz glass fragments. The substance was passed through the tube at a rate of 3-4 drops per minute. Slight carburization of the glass was observed only in the front part of the tube. Part of the acetate was reobtained unchanged. The condensate was freed from acetic acid by washing with a solution of soda, and was then dried over calcined sodium sulfate and distilled under vacuum.

Dehydrogenation of hydroaromatic hydrocarbons. Dehydrogenation was carried out in an 8 cm diameter

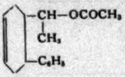
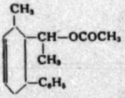
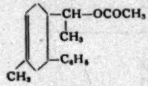
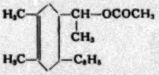
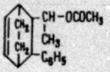
TABLE 3

Alcohols

| Substance | Boiling point at 10 mm | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ found | $MR_D$ calc. | Found % C | Found % H | Found % OH | Calc. % C | Calc. % H | Calc. % OH | Yield (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  | 152—153°,<br>т. пл.<br>127—128° | 1.0430 | 1.5538 | 62.14 | 62.10 | 83.48,<br>83.13 | 9.30, 9.34 | 8.75, 8.83 | 83.13 | 8.97 | 8.40 | 80 |
|  | 159—160 | 1.0291 | 1.5465 | 66.62 | 66.73 | 83.23 | 9.80 | 8.29 | 83.28 | 9.32 | 7.86 | 70 |
|  | 163—164 | 1.0271 | 1.5461 | 66.71 | 66.73 | 83.62 | 9.68 | 7.49 | 83.28 | 9.32 | 7.86 | 90 |
|  | 171—173 | 1.0211 | 1.5448 | 71.30 | 71.34 | 83.55 | 9.86 | 7.70 | 83.42 | 9.62 | 7.35 | 75 |
|  | 173—174 | 1.0750 | 1.5625 | 68.93 | 69.14 | 84.04 | 8.82 | 7.23 | 84.17 | 8.83 | 7.44 | 35 |

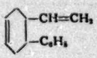
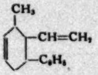
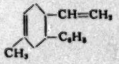
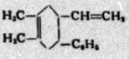
## TABLE 4

Acetates

| Substance | Boiling point at 10 mm | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ | | Found % | | Calc. % | | Yield (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | found | calc. | C | H | C | H | |
|  | 163.5—164 5°<br>— | 1.049<br>— | 1.5240<br>— | 71.26<br>— | 71.44<br>— | 78.46,<br>78.67 | 8.47,<br>8.43 | 78.66 | 8.25 | 65 |
|  | 165—166 | 1.033 | 1.5212 | 76.18 | 76.09 | 79.08,<br>79.18 | 8.22,<br>8.37 | 79.00 | 8.58 | 80 |
|  | 167 | 1.0335 | 1.5225 | 76.30 | 76.09 | 78.88,<br>79.29 | 8.43,<br>8.38 | 79.03 | 8.58 | 63 |
|  | 175—177 | 1.026 | 1.5222 | 81.00 | 80.71 | 79.54,<br>79.40 | 9.08,<br>9.19 | 79.37 | 8.88 | 67 |
|  | 177—178 | 1.0682 | 1.5358 | 78.90 | 78.51 | 80.9,<br>79.86 | 8.52.<br>8.41 | 79.97 | 8.20 | 48 |

## TABLE 5

Hydrocarbons

| Substance | Boiling point at 10 mm | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ | | Found % | | Calc. % | | Yield (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | found | calc. | C | H | C | H | |
|  | 123—125° | 0.9714 | 1.5492 | 60.36 | 60.12 | 90.99,<br>91.35 | 8.51,<br>8.71 | 91.25 | 8.75 | 50 |
|  | 132—134 | 0.9638 | 1.5415 | 64.70 | 64.73 | 91.15,<br>91.05 | 9.35,<br>9.40 | 90.85 | 9.15 | 60 |
|  | 130—131.5 | 0.9654 | 1.5451 | 64.95 | 64.73 | 91.00,<br>90.90 | 9.53,<br>9.45 | 90.85 | 9.15 | 55 |
|  | 144—145 | 0.9640 | 1.5447 | 69.61 | 69.34 | 90.68,<br>90.83 | 9.84,<br>9.80 | 90.51 | 9.49 | 61 |

glass tube and a layer of catalysts 18 cm long, heated by a vertical electrical oven to 340-360°. The substance was introduced at a rate of 3-4 drops per minute. Platinized charcoal (10% platinum), prepared by Linstead's method [15], served as the catalyst. After 4-methyl-1-vinyl-2-phenyl-4-cyclohexene had been passed through the tube twice, 5-methyl-2-ethyldiphenyl was obtained.

B.p. 138-140° at 10 mm, $d^{20}_{4}$ 0.9886, $n^{20}_{D}$ 1.5745, $MR_D$ 65.70; calc. 64.27.

Found %: C 91.54, 91.62; H 8.02, 8.09. $C_{15}H_{16}$. Calculated %: C 91.79; H 8.21.

## SUMMARY

1. The condensation of cinnamaldehyde with divinyl, piperylene, isoprene, diisopropenyl, 1,3-cyclohexadiene and 1,3-cyclopentadiene was investigated and the condensation products were described.

2. By the action of methylmagnesium iodide on 2-phenyltetrahydrobenzaldehyde and its homologs secondary hydroaromatic alcohols were obtained and described and the acetates of the latter were prepared.

3. The corresponding hydroaromatic hydrocarbons were obtained by the pyrolysis of all the acetates with the exception of the acetate of methyl-(2-phenyl-3,6-endoethylene-cyclohexene-4-yl)-carbinol.

4. From the example of 4-methyl-1-vinyl-2-phenyl-4-cyclohexene it was shown that in accordance with the proposed structure hydrocarbons of the given type are dehydrogenated on platinum.

## LITERATURE CITED

[1] A. A. Petrov and N. P. Sopov, J. Gen. Chem. 22, 591 (1952).*

[2] A. A. Petrov and N. P. Sopov, J. Gen. Chem. 22, 890 (1952).*

[3] A. A. Petrov and N. P. Sopov, J. Gen. Chem., Symp. I, 379 (1953).*

[4] N. P. Sopov, J. Gen. Chem. 25, 2082 (1955).*

[5] N. P. Sopov, J. Gen. Chem. 26, 1602 (1956).*

[6] A. A. Petrov and N. P. Sopov, J. Gen. Chem. 26, 2452 (1956).*

[7] O. Diels and K. Alder, Lieb. Ann. 470, 62 (1929).

[8] Fujise, Horiuti and Takahashi, Ber. 69, 2102 (1936).

[9] E. Bergmann and F. Bergmann, J. Am. Chem. Soc. 59, 1443 (1937).

[10] E. G. Kataev, N. M. Beksheneva, Scientific Records Kazan Univ., 115, No. 3, 13-19 (1955).

[11] V. Eranzen and H. Krauch, Chem. Ztg. 79, 548 (1955).

[12] W. J. Bailey and C. J. King, J. Am. Chem. Soc. 77, 75 (1955).

[13] W. J. Bailey, J. J. Hewitt and C. J. King, J. Am. Chem. Soc. 77, 357 (1955).

[14] Dictionary of Org. Comp., Foreign Lit. Press, (1949) [Russian translation].

[15] R. P. Linstead, K. O. A. Michaolis and S. L. S. Thomas, J. Chem. Soc. 1940, 1138.

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# SYNTHESIS OF β-CHLORO SUBSTITUTED ALCOHOLS AND THEIR CONVERSIONS

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β-Chloro substituted alcohols, in which the chlorine is in a position β to the hydroxyl group (β-chlorohydrins), have been difficultly accessible and unstudied until now.

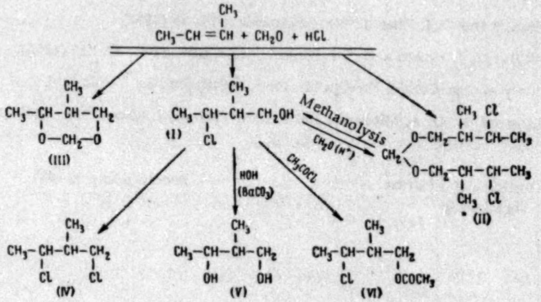
When olefins are reacted with formaldehyde in an aqueous medium in the presence of dilute acids, the main reaction products are alkyldioxanes-1,3 in yields of 70-90% based on the formaldehyde reacted [1].

The present work is devoted to a detailed investigation of the reaction of simple olefins (ethylene, propylene and butylenes) with formaldehyde in concentrated hydrochloric acid. In the first instance we were interested in the reactions of butylenes since we hoped to use the products obtained for some syntheses of practical importance.

In the liquid phase, butene-2 reacts with formaldehyde (in the form of paraform). dissolved in concentrated hydrochloric acid, quite vigorously, even at room temperature (25°). Here the main reaction product is the formal of the corresponding β-chlorohydrin,– 3-chloro-2-methylbutanol (II), which is obtained in 52.9% yield on the formaldehyde reacted,* and 4,5-dimethyldioxane-1,3 (III) (31.6%). The chlorohydrin itself (I) was obtained in only low yield (9.17%).

The structure of the β-chlorohydrin (I) was established by the following reactions: 1) treatment of (I) with thionyl chloride gave 1,3-dichloro-2-methylbutane (IV) in quantitative yield; 2) hydrolysis of (I) in the presence of barium carbonate gave 2-methylbutanediol-1,3 (V) and 3) acetylation of (I) with acetyl chloride gave the acetate of 3-chloro-2-methylbutanol-1 (VI) in 80-85% yield.

That (II) had the structure of the formal of the β-chlorohydrin (I) was demonstrated by the fact that hydrolysis in the presence of methanol (methanolysis) gave a quantitative yield of the β-chlorohydrin (I). In this case the methanol was used to bind the formaldehyde liberated during the hydrolysis as methylal and to shift the equilibrium completely in the direction of the formation of the chlorohydrin [2]. On the other hand, treatment of the β-chlorohydrin (I) with formaldehyde in an acid medium gave the formal (II). All the conversions given are illustrated by scheme 1.



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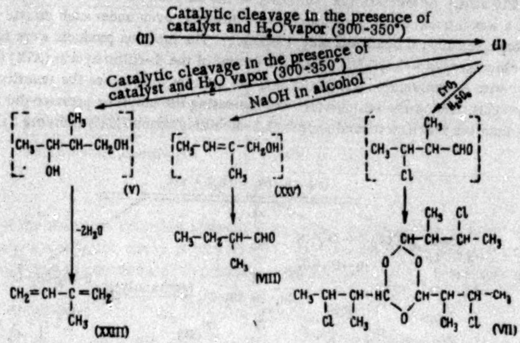
* From here on the yields in brackets are calculated on the formaldehyde reacted.

We also investigated some conversions of the β-chlorohydrin (I) and its formal (II). Passing (I) and (II) at 300-350° over a phosphate-type catalyst in the presence of water vapor gave isoprene in 53.1% yield (for I) and 56.1% (for II) on the material passed. Catalysts of this type, which were proposed for skeletal cleavage of alkyldioxanes into dienes by one of us (together with G. I. Kishinskii [11]), possess hydrolyzing and dehydrating properties. Apparently, on the catalyst there is the successive hydrolysis of formal (II) into β-chlorohydrin (I) and hydrolysis of (I) into diol (V); the diol is then dehydrated into isoprene (XXIII) with the loss of two molecules of water (scheme 2).


Catalytic cleavage in the presence of catalyst and H₂O vapor (300-350°)
(II)
(I)
Catalytic cleavage in the presence of catalyst and H₂O vapor (300-350°)
NaOH in alcohol
CrO₃ H₂SO₄
(V)
-2H₂O
(XXIII)
(XXV)
(VIII)
(VII)

Oxidation of the β-chlorohydrin (I) with chromium trioxide in sulfuric acid gave the trimer of 3-chloro-2-methylbutanol (VII). Apparently, in this case the hydroxyl group of the β-chlorohydrin (I) was oxidized to an aldehyde group; in the presence of acid, the aldehyde formed was then converted into the trimer (VII).

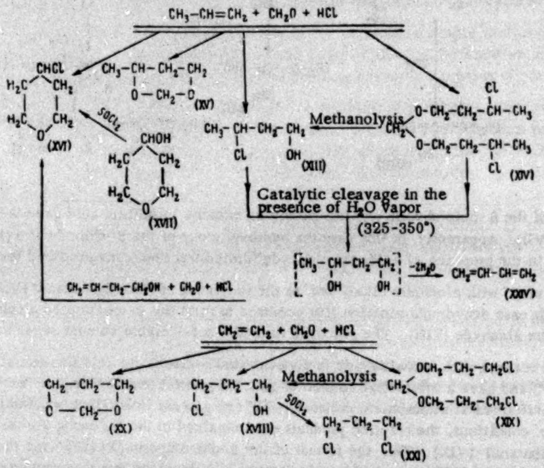
Treatment of (I) with alcoholic alkali led to the formation of 2-methylbutanal (VIII), but in low yield. Apparently, in this case dehydrochlorination first occurred to form the β-unsaturated alcohol (XXV), which then isomerized into the aldehyde (VIII). The aldehyde formed a considerable amount of tar in the presence of alkali.

Isobutylene reacted with formaldehyde in concentrated hydrochloric acid solution at a considerably greater rate than butene-2 and gave a substantial amount of tar. To prevent undesirable side reactions, the reaction with isobutylene was performed at atmospheric pressure at 10° and gaseous isobutylene was fed into the reaction mixture. Under these conditions, the reaction products were obtained in the following yields: β-chlorohydrin — 3-chloro-3-methylbutanol-1 (IX) (3%); the formal of the β-chlorohydrin (X) (28%) and the alkyldioxane — 4,4-dimethyldioxane-1,3 (XI) (53%). A considerable amount of isobutylene was thus converted into tertiary butyl chloride (XII). The β-chlorohydrin (IX) and its formal (X), obtained from isobutylene, were unstable and gave off hydrogen chloride during storage. Apparently, a substantial lowering in the stability of the bond between the chlorine and the tertiary carbon atom occurs here.

We reacted propylene with formaldehyde in concentrated hydrochloric acid solution under the same conditions as for butene-2 (the pressure in the autoclave was correspondingly higher). In this case the reaction proceeded at a slightly lower rate. Here the main reaction products were also the β-chlorohydrin — 3-chlorobutanol-1 (XIII) (7%), the formal of the β-chlorohydrin (XIV) (36%) and 4-methyldioxane-1,3 (XV) (27%). In addition, a substance was found in the reaction products, which we characterized as 4-chlorotetrahydropyran (XVI) (8%). The structures of (XIII) and (XIV) were established in the same way as for the analogous products obtained in the reaction with butene-2. The formal (XIV) was smoothly converted into the β-chlorohydrin (XIII) by methanolysis. To prove the structure of (XVI), we synthesized 4-hydroxytetrahydropyran (XVII) from allylcarbinol and formaldehyde by the method which one of us described previously [3]; the latter was treated with thionyl chloride to give 4-chlorotetrahydropyran, which was identical with the product (XVI) we obtained. In addition, from allylcarbinol and formaldehyde in concentrated hydrochloric acid solutions we also synthesized 4-chlorotetrahydropyran, identical with (XVI).

Catalytic cleavage of the β-chlorohydrin (XIII) and its formal (XIV) in the presence of water vapor over the catalysts mentioned above led to the formation of divinyl in 85% yield on the material decomposed and 80% on that passed. Dehydrochlorination of the β-chlorohydrin with alcoholic alkali led to the formation of allylcarbinol and butyraldehyde in low yields. The mechanism of the latter reactions is apparently the same as for the products from butene-2. The reactions for propylene are given in scheme 3.

The reaction of ethylene with formaldehyde in concentrated hydrochloric acid solution was most difficult of all. In this case we performed it at a considerably higher temperature (75°) and the initial pressure of ethylene in the autoclave was 110 atm.; to increase the solubility of the ethylene, a volume of chloroform equal to that of the reaction mixture was introduced into the autoclave. However, even under such drastic conditions the amount of formaldehyde consumed after 4 hours was only 47-50%. The reaction products were found to contain the β-chlorohydrin – 3-chloropropanol-1 (XVIII) (5%), the formal of the β-chlorohydrin (XIX) (37%) and dioxane-1,3 (XX) (7%) together with a considerable amount of tar. An attempt to increase the reaction rate by adding zinc chloride (10% by weight), raising the temperature and increasing the ethylene pressure did not lead to better yields in addition, in this case the reaction tended to form 1,3-dichloropropane (XXI) (scheme 3).


$CH_3-CH=CH_2 + CH_2O + HCl$
(XVI)
(XV)
$SOCl_2$
(XVII)
(XIII)
Methanolysis
(XIV)
Catalytic cleavage in the presence of $H_2O$ vapor
(325-350°)
$-2H_2O$
$CH_2=CH-CH=CH_2$
(XXIV)
$CH_2=CH-CH_2-CH_2OH + CH_2O + HCl$
$CH_2=CH_2 + CH_2O + HCl$
(XX)
(XVIII)
Methanolysis
$SOCl_2$
(XIX)
(XXI)

To study the relative reaction rates for the reactions of propylene, butene-2 and isobutylene with formaldehyde in concentrated hydrochloric acid solution, we devised special experiments. They were performed at –5° (i.e., at a temperature at which the reactions proceeded at a moderate rate) and with constant initial concentrations of olefin, formaldehyde and hydrochloric acid. Since these reactions were proceeding in a system composed of two immiscible liquid phases (hydrochloric acid solution of formaldehyde and hydrocarbon phase), we first determined the stirring rate at which the reactions were not limited by diffusion factors. It was thus found that the reaction rate could be represented satisfactorily by a first-order equation in all cases.

Curves of the change in the degree of formaldehyde conversion with time at –5° are given in the Figure for all three olefins. To determine the activation energy and the temperature coefficient of the reactions, additional experiments were performed at –15° for isobutylene, + 5° for butene-2 and propylene and + 15° for propylene. The table shows the rate constants for the three olefins at different temperatures. Using these data and Arrhenius' equation, the activation energies and the temperature coefficients of the reactions were determined (at temperatures close to 0°).

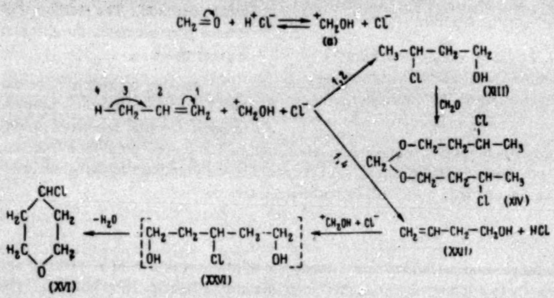
Thus, the rates of conversion of the three given olefins were related in the following way: propylene: butene-2 : isobutene – 1 : 1.2 : 18.5.

## TABLE

Rate Constants and Activation Energies of the Reactions Between Propylene, Butene-2 and Isobutylene and Formaldehyde in Concentrated Hydrochloric Acid.

| Temperature | Reaction rate constant (min$^{-1}$) $K \cdot 10^3$ | | |
|---|---|---|---|
| | isobutylene | butene-2 | propylene |
| −15° | 47.35 | — | — |
| −5 | 108.52 | 5.88 | 4.88 |
| +5 | — | 13.83 | 11.52 |
| +15 | — | — | 21.72 |
| Activation energy (kcal/mole) | 10950 | 12156 | 12200 |
| Temperature coefficient | 2.48 | 2.35 | 2.36 |

The mechanism of the reactions described above is a particular case of the mechanism of the reaction between olefins and formaldehyde, which one of us proposed [1]. It is represented by scheme 4, where the reaction of propylene and formaldehyde in concentrated hydrochloric acid is considered as an example (scheme 4).



$CH_2{=}O + H^+Cl^- \rightleftharpoons {}^+CH_2OH + Cl^-$
(a)
4 3 2 1
$H-CH_2-CH=CH_2 + {}^+CH_2OH + Cl^-$
1,2
1,4
$CH_3-CH(Cl)-CH_2-CH_2OH$
(XIII)
$CH_2O$
$CH_2(O-CH_2-CH_2-CH(Cl)-CH_3)_2$
(XIV)
$CH_2{=}CH-CH_2-CH_2OH + HCl$
(XXII)
$^+CH_2OH + Cl^-$
$CH_2(OH)-CH_2-CH(Cl)-CH_2-CH_2(OH)$
(XXVI)
$-H_2O$
CHCl
$H_2C$
$CH_2$
O
(XVI)

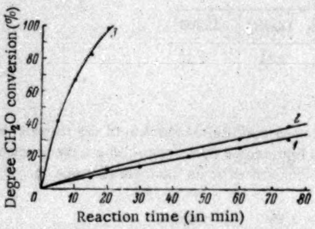
Propylene (and also butene-2) is characterized by the presence of $\sigma,\pi$-conjugation, which gives it a capacity for dual reaction at the 1,2 and the 1,4 bonds [4]. In the reaction with formaldehyde and hydrochloric acid, an intermediate carbonium ion (a) and a chloride ion are formed. Heterolytic addition to the olefin then occurs and the carbonium ion (a) is attached to the first carbon atom, which has the highest electron density. Thus, as a result of 1,2 addition, the β-chlorohydrin (XIII) is formed. In the case of reaction at the 1,4 position, the addition of the carbonium ion to the first carbon atom is accompanied by transfer of the reaction center to the fourth atom. The hydrogen atom is thus protonized and eliminated as HCl, which produces rupture of the 3,4 bond and establishes a new 2,3 π-bond. In this way the reaction leads to the formation of the allylcarbinol (XXII). The β-chlorohydrin (XIII) and the allylcarbinol (XXII) formed then react with formaldehyde when (XIII) forms the linear formal (XIV) and (XXII) forms the chloropentanediol (XXVI); the latter readily loses water to close a six-membered ring forming 4-chlorotetrahydropyran(XVI). In the case of the reaction with butylenes, there is only 1,2-addition. The formation of a considerable amount of alkyldioxanes in addition to β-chlorohydrins and their derivatives, observed in reactions with all the olefins, is explained by interaction of the olefin with formaldehyde in an acid aqueous medium [1].

The different reactivities of the olefins (propylene, isobutylene and butene-2) in this reaction and the ratio of their reaction rates are characteristic of many heterolytic addition reactions to these olefins and are explained by the peculiarities of their structures. The sharp increase in the rate of these reactions for isobutylene is generally known, as its double bond is strongly polarized by the action of the two electron-donor methyl groups and its molecule therefore has a considerable dipole moment. Butene-2 has no dipole moment due to the symmetry of its structure; however, the dynamic effect of the $\sigma,\pi$-conjugation, connected with redistribution of electron density under the action of the attacking agent, apparently has a considerable effect here. As a result of this, the rate of heterolytic reactions is always slightly greater for non-polar (in the static state) butene-2 than for polar propylene.

## EXPERIMENTAL

### A. The Reaction of Olefins With Formaldehyde in Concentrated Hydrochloric Acid Solution

The reactions with butene-2, propylene and ethylene were performed in a copper-plated autoclave of 1.5 liters capacity. The reaction with isobutylene was performed in a three-necked flask, fitted with a mechanical stirrer, a thermometer and a reflux condenser. For all the experiments, the paraformaldehyde was first dissolved in concentrated hydrochloric acid (37%) allowing 1 mole of $CH_2O$ to 2 moles of HCl. The paraformaldehyde was dissolved at 50-70° on a water bath. After removal of the unreacted olefin, the reaction mixture was poured into a separating funnel. The oily layer was separated and the aqueous acid layer extracted with dichloroethane (or chloroform). The combined oily layers were then neutralized with 3-5% soda solution, washed with water and dried by distilling off the water as an azeotrope with dichloroethane. The residue was vacuum-distilled. To isolate pure products, the distillation was performed several times.



Reaction rates of the three olefins with formaldehyde in hydrochloric acid at −5°: 1) propylene; 2) butene-2; 3) isobutylene.

Starting materials. For the reactions we used a 99% isobutylene fraction, prepared by dehydration of isobutyl alcohol, butene-2 (99%), prepared by fractionation of a mixture of butenes on a semi-industrial column of 100 plates, propylene fraction, containing $C_3H_6$ (87%), $C_3H_8$ (13%), and ethylene (99.8%) (from a tank) prepared by dehydrating ethyl alcohols, and formaldehyde in the form of paraformaldehyde with a 95-96% formaldehyde content.

### B. Methanolysis of Formals

The methanolysis was performed in the presence of hydrochloric acid as catalyst and excess methyl alcohol. The reaction vessel was a round-bottomed flask connected to a fractionation column. The distillate collected consisted of the azeotrope of methylal and methanol and part of the excess methanol. The residue in the distillation flask after hydrolysis was diluted with dichloroethane, neutralized with 3% soda solution and washed with water. After azeotropic drying, the hydrolysis product was vacuum-distilled.

### C. Reaction With Butene-2

The autoclave was loaded with 80.5 g $CH_2O$, 177.4 g HCl (in the form of a 37% solution) and 190 g of butene-2. The autoclave was rocked at 25° for 50 minutes. The reaction products were treated by procedure A. The formaldehyde consumed was 87%. As a result of the experiment we obtained 3-chloro-2-methylbutanol-1 (I),* the formal of 3-chloro-2-methylbutanol-1 (II)* and 4,5-dimethyldioxane-1,3 (III).

1) 3-Chloro-2-methylbutanol-1 (I)*, 26.28 g (9%).

B.p. 79.9° (20 mm), $n^{20}$D 1.4509, $d^{20}_4$ 1.04512, $MR_D$ 31.55; calc. 31.58.

Found %: C 49.01; H 8.89; Cl 28.86; OH 13.2 (phthalylation). $C_5H_{11}OCl$. Calculated %: C 48.97; H 8.98; Cl 28.97; OH 13.87.

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*The compounds marked with an asterisk, here and below, were obtained for the first time by us.

1,3-Dichloro-2-methylbutane (IV). 30 ml of the $\beta$-chlorohydrin (I) was added dropwise at room temperature to 30 ml of $SOCl_2$ in a flask fitted with a reflux condenser and a dropping funnel. The excess thionyl chloride was distilled off and the residue distilled to give compound (IV).

B.p. 80.1-80.5°, $n^{20}D$ 1.4502, $d^{20}_4$ 1.09381, $MR_D$ 34.77; calc. 35.024.

Found %: Cl 49.67. M 141.5. $C_5H_{10}Cl_2$. Calculated %: Cl 50.35. M 141.

2-Methylbutanediol-1,3 (V). Into a flask fitted with a stirrer, a thermometer and a reflux condenser, was placed 160 g of $BaCO_3$, 500 g of water and 70 g of the $\beta$-chlorohydrin (I). The reaction mixture was boiled and stirred continuously for 22 hours. We obtained 17.0 g of (V).

B.p. 89.5-90.5° (6 mm), $n^{20}D$ 1.4478, $d^{20}_4$ 0.9945.

Found %: OH 29.8 (phthalylation). $C_5H_{12}O_2$. Calculated %: OH 32.7. Literature data [2]: b.p. 92° (6 mm), $n^{20}D$ 1.4478, $d^{20}_4$ 0.9919.

Acetate of 3-chloro-2-methylbutanol-1 (VI).* 50 g of the $\beta$-chlorohydrin (I) was dissolved in 50 ml of ether and 50 ml of pyridine. The mixture was cooled to 0° and 50 g of acetyl chloride added over a period of 2 hours with stirring and cooling. The mixture was stored overnight and then treated with ice and ether. The hydrocarbon layer which appeared was separated, washed with 3% HCl, 3% $Na_2CO_3$ and water and dried over $CaCl_2$. The ether was removed and the residue vacuum-distilled. The experiment yielded compound (VI).

B.p. 78-80° (12 mm), $n^{20}D$ 1.4365, $d^{20}_4$ 1.0398, $MR_D$ 41.16; calculated 41.047.

Found %: Cl 21.61; acetyl number 1.15. $C_7H_{13}O_2Cl$. Calculated %: Cl 21.58; acetyl number 1.0.

The trimer of 3-chloror-2-methylbutanal (VII)* was prepared by oxidizing the $\beta$-chlorohydrin (I) with chromium trioxide. We used 60 g of the $\beta$-chlorohydrin (I), 45 g of $CrO_3$ in 60 ml of water and 71.6 g of $H_2SO_4$ in 138 ml of water. The $\beta$-chlorohydrin (I), cooled to 0°, was placed in a flask fitted with a reflux condenser, a thermometer and a dropping funnel, and the cooled $H_2SO_4$ solution added to it. The $CrO_3$ solution was added portionwise to the cooled mixture obtained over a period of 2.5 hours. The temperature of the reaction mixture varied from 0° to +5°. The reaction mixture was then diluted with ice water and extracted with ether. The ether extract was dried with $CaCl_2$. Evaporation of the ether on a water bath yielded 36 g of residue, which was distilled to give compound (VII).

B. p. 130.1° (10 mm), $n^{20}D$ 1.4600, $d^{20}_4$ 1.10988, $MR_D$ 89.33; calc. 88.80.

Found %: Cl 29.61. M 362. $C_{15}H_{27}O_3Cl_3$. Calculated %: Cl 29.46. M 361.5.

Heating the product with Tollens' reagent gave a silver mirror.

2-Methylbutanal (VIII). 15 g of NaOH in 100 ml of alcohol was added to 43.5 g of the $\beta$-chlorohydrin (I) in 45 ml of ethyl alcohol. The mixture was heated in a flask with a reflux condenser for 45 minutes at 50°. The precipitate was filtered off and the excess alkali neutralized with $H_2SO_4$. Distillation of the reaction products yielded a fraction: b.p. 75-92° (8 g) with a 50% 2-methylbutanal content (according to analysis with hydroxylamine hydrochloride).

The product gave a silver mirror with Tollens' reagent.

The 2,4-dinitrophenylhydrazone had m.p. 126.5°. A mixed melting point with the 2,4-dinitrophenylhydrazone of 2-methylbutanal, prepared by another method, was not depressed. Literature data [5]: m.p. 120.5°.

2) Formal of 3-chloro-2-methylbutanol-1 (II), 105.8 g (52.9%).

B.p. 127.5° (5-6 mm), $n^{20}D$ 1.4561, $d^{20}_4$ 1.0624, $MR_D$ 66.28; calc. 66.018.

Found %: Cl 27.60. M 259. $C_{11}H_{22}O_2Cl_2$. Calculated %: Cl 27.62. M 257.

Compound (II) was subjected to methanolysis by procedure B. 50 g of formal (II), 25 g of methanol and 5 ml of HCl (37%) were used. The methanolysis yielded 13.6 g of methylal and 38.22 g of the $\beta$-chlorohydrin (I). The formal (II) was also prepared directly from $CH_2O$ and the $\beta$-chlorohydrin (I). A mixture of 30 g of the $\beta$-chlorohydrin (I), 3.7 g of paraformaldehyde and 0.7 g of $H_2SO_4$ (d 1.84) was heated in a flask with a reflux condenser for 2 hours. The mixture was cooled and then diluted with ethyl ether. The ether layer was separated, neutralized with 3% NaOH and dried with $CaCl_2$. Distillation yielded 10.4 g of (II).

Isoprene (XXIII). The catalytic cleavage of the β-chlorohydrin (I) and its formal (II) was carried out over a catalyst in a laboratory contact furnace. Thus, under the best conditions 300°, contact time 0.5 sec and dilution of (I) with water vapor in a ratio of 1 : 3 by volume (I) gave isoprene in 53.1% yield on the material passed and 84.2% on that decomposed. Under the same conditions, the formal (II) gave isoprene in a yield of 56.1% on the material passed and 78.8% on that decomposed. The isoprene was characterized by its physical constants and identified as its adduct with maleic anhydride with m.p. 62°.

3) 4,5-Dimethyldioxane-1,3 (III), 42.7 g (31.60%).

B. p. 131-132°, $n^{20}_D$ 1.4230, $d^{20}_4$ 0.9620.

Literature data [1]: b.p. 133°, $n^{20}_D$ 1.4229, $d^{20}_4$ 0.9618.

### D. Reaction With Isobutylene

For the experiment we used 62.6 g of $CH_2O$, 152 g of HCl (as a 37% solution) and 300 g of isobutylene. The reaction mixture was stirred and the isobutylene added over a period of 3.5 hours at 10°. The formaldehyde consumed under these conditions reached 95%. The reaction products were treated by procedure A. The experiment yielded the following substances: 3-chloro-3-methylbutanol-1 (IX),* the formal of 3-chloro-3-methylbutanol-1 (X)* and 4,4-dimethyldioxane-1,3 (XI).

1) 3-Chloro-3-methylbutanol-1,* 6.86 g (2.8%).

B. p. 77-79° (16 mm), $n^{20}_D$ 1.4461, $d^{20}_4$ 1.03566, $MR_D$ 31.547; calc. 31.682.

Found %: Cl 29.2; OH 10.59. (phthalylation). $C_5H_9OCl$. Calculated %: Cl 28.97; OH 13.85.

1,3-Dichloro-3-methylbutane was obtained by treating the β-chlorohydrin (IX) with thionyl chloride.

B. p. 79-82° (80 mm), $n^{20}_D$ 1.4562 (1.4570), $d^{20}_4$ 1.11446.

2) Formal of 3-chloro-3-methylbutanol-1 (X),* 46.52 g (27.7%).

B. p. 140-142° (15 mm), $n^{20}_D$ 1.4511, $d^{20}_4$ 1.0387, $MR_D$ 66.63; calc. 66.018.

Found %: Cl 27.47. $C_{11}H_{22}O_2Cl_2$. Calculated %: Cl 27.60.

3) 4,4-Dimethyldioxane-1,3 (XI), 62.16 g (53.6%).

B. p. 133° (760 mm), $n^{20}_D$ 1.4235, $d^{20}_4$ 0.9630. Literature data [2]: b.p. 133°, $n^{20}_D$ 1.4238, $d^{20}_4$ 0.9634.

### E. Reaction With Propylene

The autoclave was loaded with 70.86 g of $CH_2O$, 172 g of HCl (as a 37% solution) and 289 g of propylene fraction. The autoclave was rocked at 25° for 60 minutes. The formaldehyde consumed was 90.35%. The reaction products were treated by procedure A. As a result of the experiment we obtained 3-chlorobutanol-1 (XIII), the formal of 3-chlorobutanol-1 (XIV),* 4-methyldioxane-1,3 (XV) and 4-chlorotetrahydropyran (XVI).*

1) 3-Chlorobutanol-1 (XIII), 16.67 g (7.20%).

B. p. 69° (17 mm), $n^{20}_D$ 1.4428, $d^{20}_4$ 1.0641, $MR_D$ 27.019; calc. 27.064.

Found %: Cl 32.1; OH 14.65. (phthalylation). $C_4H_9OCl$. Calculated %: Cl 32.7; OH 15.65.

The acetate of 3-chlorobutanol-1* was prepared in 85% yield.

B. p. 75-76° (20 mm), $n^{20}_D$ 1.4286, $d^{20}_4$ 1.0659, $MR_D$ 36.36; calc. 36.429.

Found %: Cl 23.7; acetyl number 1.1. $C_6H_{11}O_2Cl$. Calculated %: Cl 23.6; acetyl number 1.0.

1,3-Dichlorobutane was prepared in quantitative yield by treating the β-chlorohydrin (XIII) with thionyl chloride.

B. p. 131-133° (760 mm), $n^{20}_D$ 1.4430, $d^{20}_4$ 1.11174, $MR_D$ 30.29; calc. 30.406.

Found %: Cl 55.2. M 127.9. $C_4H_8Cl_2$. Calculated %: Cl 55.9. M 127.0. Literature data [6]: b.p. 134 (131-133°), $n^{20}D$ 1.445, $d^{20}_4$ 1.1158.

Dehydrochlorination of the β-chlorohydrin (XIII) with alcoholic alkali gave allylcarbinol and butyraldehyde. In the experiment 50 g of the β-chlorohydrin (XIII) and 20 g of NaOH in 250 ml of alcohol were used. Distillation of the reaction products gave two fractions. The 1st fraction had b.p. 77-78° and gave a silver mirror with Tellens' reagent. The 2,4-dinitrophenylhydrazone obtained had m.p. 122.1°. Literature data [10] gives m.p. 122° for the m.p. of the 2,4-dinitrophenylhydrazone of butyraldehyde. A mixed melting point with the 2,4-dinitrophenylhydrazone of butyraldehyde was not depressed. The 2nd fraction with b.p. 80-98° was acetylated by the method for (I). Distillation of the acetylation products gave the acetate of allylcarbinol. The b.p. was 128-130° (760 mm) $n^{20}D$ 1.4150. The acetate content of the fraction with b.p. 128-130°, determined by titration with bromide-bromate solution, was 100.4%; the acetyl number was 1.0.

2) Formal of 3-chlorobutanol-1 (XIV),* 50.98 g (36.8%).

B.p. 131.5° (16.5 mm), $n^{20}D$ 1.4499, $d^{20}_4$ 1.08075, $MR_D$ 56.54; calc. 56.782.

Found %: Cl 31.05. $C_9H_{18}O_2Cl_2$. Calculated %: Cl 31.0.

The methanolysis of (XIV) was performed by procedure B. In the experiment 100 g of (XIV), 56.4 g of $CH_3OH$ and **ml of 37% HCl were used. The methanolysis gave 32.0 g of methylal and 76.1 g of the β-chlorohydrin (XIII).

Divinyl (XXIV). The catalytic cleavage of the β-chlorohydrin (XIII) and its formal (XIV) was performed in a laboratory contact furnace over the catalyst used for the cleavage of alkyldioxanes. Thus, under the optimal conditions [325°, contact time 0.75 sec and dilution of the β-chlorohydrin (XIII) with water vapor in the ratio of 1 : 3 by volume] the yield of divinyl on the (XIII) decomposed was 94.5% and the divinyl yield on the chlorohydrin passed was 77.8%; for the formal (XIV), the divinyl yield was 94.4% on the material decomposed and 80% on that passed under the same conditions.

3) 4-Methyldioxane-1,3 (XV), 29.44 g (27.1%).

B. p. 114° (760 mm), $n^{20}D$ 1.4155, $d^{20}_4$ 0.9762. Literature data [2]: b.p. 115.3° (760 mm), $n^{20}D$ 1.4159, $d^{20}_4$ 0.9758.

4) 4-Chlorotetrahydropyran (XVI),* 10.13 g (7.8%).

B. p. 47° (17 mm), $n^{20}D$ 1.4612, $d^{20}_4$ 1.1157, $MR_D$ 29.64; calc. 29.60.

Found %: Cl 29.2. $C_5H_9OCl$. Calculated %: Cl 29.45.

Compound (XVI) was also prepared by treating 4-hydroxytetrahydropyran (XVII) with thionyl chloride. For the experiment we used 42 g of (XVII) in 50 ml of chloroform and 50 ml of thionyl chloride in 50 ml of chloroform. The reaction mixture was heated and shaken periodically for 4 hours. The yield of compound (XVI) was 15%. Compound (XVI) was also prepared by another method – from allylcarbinol, $CH_2O$ and HCl. Into a flask fitted with a stirrer, a reflux condenser, a thermometer and a dropping funnel, was placed 88.2 g of $CH_2O$ and 0.214 g of HCl. The mixture obtained was stirred at 8°, 184 ml of allylcarbinol was slowly added and then the mixture stirred for a further 20 minutes. The total duration of the experiment was 2 hours. 86.6% of the $CH_2O$ was consumed. The reaction products yielded 46 g of (XVI).

### F. Reaction With Ethylene

The autoclave was loaded with 81.39 g of $CH_2O$, 198 g of HCl (in the form of a 37% solution) and an equal volume of chloroform. Ethylene was added until the reaction mixture was saturated with ethylene at 25° and 65 atm. Mixing was continued for 4 hours at 75° and 110 atm. The fomaldehyde consumed was 47%. The reaction products were treated by method A. The experiment yielded 3-chloropropanol-1 (XVIII), the formal of 3-chloropropanol-1 (XIX),* and dioxane-1,3 (XX).

1) 3-Chloropropanol-1 (XVIII), 5.68 g (4.77%).

B. p. 65.5-66.5° (20 mm), $n^{20}D$ 1.4450, $d^{20}_4$ 1.12165, $MR_D$ 22.42; calc. 22.446.

Found %: Cl 37.6; OH 17.1 (phthalylation). $C_3H_7OCl$. Calculated %: Cl 37.56; OH 18.0. Literature data [7]: b.p. 161-162°, $n^{20}D$ 1.44693, $d^{20}_4$ 1.1309.

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**Omitted, as in Russian – Publisher's note.

1,3-Dichloropropane (XXI) was prepared by the procedure for the preparation of the dichloride from the β-chlorohydrin (I). For the experiment we used 5.0 g of the β-chlorohydrin (XVIII) and 7.7 g of thionyl chloride. Distillation yielded 4 g of (XXI).

B. p. 120°, $n^{20}D$ 1.4462, $d^{20}_4$ 1.17166, $MR_D$ 25.72; calc. 25.788.

Found %: Cl 62.9. $C_3H_6Cl_2$. Calculated %: Cl 62.8. Literature data [8]: b.p. 120.4°, $d^{16}_4$ 1.1896.

2) Formal of 3-chloropropanol-1 (XIX), 31.41 g (37.1%).

B. p. 85.5-87.5° (2 mm), $n^{20}D$ 1.4540, $d^{20}_4$ 1.14458, $MR_D$ 47.55; calc. 47.546.

Found %: Cl 34.55. $C_7H_{14}O_2Cl_2$. Calculated %: Cl 34.8.

The methanolysis of (XIX) was performed by procedure B. In the experiment 49.7 g of (XIX), 3.5 g of $CH_3OH$ and 6.8 g of 37% hydrochloric acid were used. The reaction yielded 7.0 g of (XVIII).

3) Dioxane-1,3 (XX), 4.19 g (7.58%).

B. p. 105-107° (758 mm), $n^{20}D$ 1.4220, $d^{20}_4$ 1.0849. Literature data [9]: b.p. 105° (755 mm), $n^{20}D$ 1.41652, $d^{20}_4$ 1.03422.

### Investigation of the Relative Reaction Rates in the Interaction of Olefins with Formaldehyde in Concentrated Hydrochloric Acid Solution

The experiments were performed in copper ampules of 10 ml capacity. Several ampules were placed simultaneously in a rocking thermostat, filled with circulating industrial brine. The temperature in the thermostat was regulated by the brine input. After 3 minutes mixing, the "blank ampule" was removed. The contents of the ampule were poured into water and the amount of formaldehyde determined. The amount of formaldehyde in the blank ampule was taken as the initial amount. Subsequent ampules were removed after definite time intervals and for each ampule. The formaldehyde content was determined and the percent used calculated.

## SUMMARY

1. A study was made of the interaction of simple olefins with formaldehyde in concentrated hydrochloric acid solution, which led to the formation of β-chlorosubstituted alcohols and their formals, together with a considerable amount of alkyldioxanes.

2. Some chemical conversions of β-chloro substituted alcohols and their formals were studied.

3. The relative reactivities of the olefins in these reactions were investigated.

4. The mechanism of these reactions was explained as a particular case of the general mechanism of the reaction of olefins with aldehydes, proposed previously.

## LITERATURE CITED

[1] M. I. Farberov, Proc. Acad. Sci. USSR 110, 1005 (1956); M. I. Farberov, Ia. I. Rotshtein, A. M. Kut'in, N. K. Shemiakina, J. Gen. Chem. 27, 2806 (1957).*

[2] M. I. Farberov, N. K. Shemiakina, J. Gen. Chem. 26, 2749 (1956).*

[3] M. I. Farberov, E. P. Tepenitsyna, N. K. Shemiakina, J. Gen. Chem. 25, 133 (1955).*

[4] A. N. Nesmeianov and M. I. Kabachnik, J. Gen. Chem. 25, 41 (1955).*

[5] Dictionary of Org. Cpds., Vol. II, pp. 640.**

[6] Dictionary of Org. Cpds., Vol. I, pp. 745.**

[7] Dictionary of Org. Cpds., Vol. I, pp. 525.**

[8] Dictionary of Org. Cpds., Vol. I, pp. 778.**

[9] Dictionary of Org. Cpds., Vol. I, pp. 1012.**

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*Original Russian pagination. See C.B. translation.

**In Russian.

[10] R. Shriner and R. Fuson, Systematic Qualitative Analysis of Organic Compounds, 225 (1950) [Russ. Trans.].

[11] M. I. Farberov et al., A New Synthesis Method for Dienes of the Divinyl Series. Min. Chem. Ind. Press, (1952). [in Russian].

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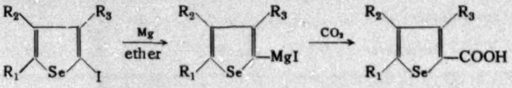
# THE CHEMISTRY OF SELENOPHENE

## XI. α-IODOSELENOPHENES IN THE ORGANOMAGNESIUM SYNTHESIS OF SELENOPHENE-α-CARBOXYLIC ACIDS

Iu. K. Iur'ev and N. K. Sadovaia

In the work of Umezawa [1], devoted to the halogenation of the selenophene nucleus, it was noted that 2-haloselenophenes and, in particular, 2-iodoselenophene hardly reacted with magnesium under the conditions of the Grignard reaction. In connection with this, in one of our previous works [2] we metalized the selenophene nucleus by treating α-iodoselenophenes with phenyllithium, in studying the reactivity of α-haloselenophenes. The α-lithiumselenophenes formed in this way gave the corresponding α-selenophenecarboxylic acids, when subsequently treated with carbon dioxide.

In the present work we established that despite the statement of Umezawa, α-iodoselenophenes are capable of undergoing a Grignard reaction and form selenienylmagnesium iodides when treated with magnesium in dry ether. However, this reaction proceeds with difficulty and requires activation with ethylene bromide and slow addition of the α-iodoselenophene to the magnesium with the ether solution boiling continuously. By carboxylation of the α-selenienylmagnesium iodides formed, we obtained the corresponding α-carboxylic acids of the selenophene series, identical with those we obtained previously [2].



2-Bromoselenophene would not undergo the reaction described; there was no reaction either in ethyl or dibutyl ether.

We measured the dissociation constants of selenophene-2-carboxylic and benzoic acids in 80% ethyl alcohol at 20°, using an LP-5 potentiometer with a glass electrode. The measurement showed the selenophene-2-carboxylic acid ($K_{diss} = 1.06 \cdot 10^{-6}$) was ten times stronger than benzoic acid ($K_{diss} = 3.26 \cdot 10^{-7}$).

## EXPERIMENTAL

Five to ten drops of an ether solution of α-iodoselenophene was added to a slightly greater amount of magnesium turnings than that required theoretically, covered with absolute ether. If the reaction did not begin, 0.5 ml of ethylene bromide was introduced and then the solution of α-iodoselenophene was added slowly dropwise (over 1.5-2 hours) while the reaction mixture was boiled continuously and stirred vigorously. The reaction mixture was cooled, treated with excess solid carbon dioxide, then decomposed with water and acidified with 5-7 drops of concentrated hydrochloric acid. The ether layer was separated and the aqueous one extracted with ether. The combined ether extracts were washed with water and dried with anhydrous sodium sulfate. When the solution was evaporated to small volume, crystals of selenophene-2-carboxylic acid were deposited and these were separated and recrystallized from water or dilute alcohol.

The results obtained in these experiments are given in Table 1.

TABLE 1

Preparation of Selenophene-α-carboxylic acids

| Reaction components* | | | Reaction products | | |
|---|---|---|---|---|---|
| α-iodoselenophenes | | | | | |
| name | amount (in g) | magnesium (in g) | selenophene-α-carboxyl acid | melting point | yield (in %) |
| 2-Iodoselenophene (b.p. 84-85° at 11 mm) | 4 | 0.5 | Selenophene-2-carboxylic acid | 119-120° | 53 |
| 2-Iodo-3-methylselenophene (b.p. 94-95° at 9 mm) | 3.9 | 0.5 | 3-Methylselenophene-2-carboxylic acid | 132-133° | 45 |
| 5-Iodo-2,4-dimethylselenophene (b.p. 110-111° at 10 mm) | 3 | 0.3 | 2,4-Dimethyl-selenophene-5-carboxylic acid | 177-178° | 50 |
| 2-Iodo-3,4-dimethylselenophene (b.p. 122-123° at 12 mm) | 5 | 0.5 | 3,4-Dimethylselenophene-2-carboxylic acid | 182.5-183 (decomp) | 52 |

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*In all the experiments, 20 ml of ether was taken.

Mixed melting points of the acids obtained in the present work and the corresponding authentic selenophene-α-carboxylic acids, which were described previously [2], were not depressed.

We determined the dissociation constants of selenophene-2-carboxylic acid. The pH measurement was performed in 80% ethyl alcohol at 20° on an LP-5 potentiometer with a glass electrode. A 0.01 molar aqueous alcohol solution of selenophene-2-carboxylic acid was 30, 50 and 70% neutralized with 0.1 N sodium hydroxide solution and the pH values of the solutions obtained were measured. The dissociation constants were calculated by the formula deduced in Kumler's work [3].

For comparison, the dissociation constant of benzoic acid was determined under the same conditions (Table 2).

TABLE 2

| Acid | $K_{diss}$ | pK |
|---|---|---|
| Selenophene-2-carboxylic . . . . . | $1.06 \cdot 10^{-6}$ | 5.98 |
| Benzoic . . . . . . . . . . . . . . . . . | $3.26 \cdot 10^{-7}$ | 6.49 |

## SUMMARY

The selenophene nucleus is metalized not only by the action of phenyllithium on α-iodoselenophenes, but also by the action of magnesium on them under Grignard reaction conditions.

Carboxylation of the α-selenienylmagnesium iodides formed by this reaction leads to selenophene-α-carboxylic acids.

The dissociation constants of selenophene-2-carboxylic and benzoic acids were determined: selenophene-2-carboxylic acid is ten times tronger than benzoic acid.

## LITERATURE CITED

[1] S. Umezawa, Bull. Chem. Soc. Japan. 14, 155 (1939).

[2] Iu. K. Iur'ev and N. K. Sadovaia, J. Gen. Chem. 26, 3154 (1956).*

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*Original Russian pagination. See C.B. translation.

[3] W. Kumler, J. Am. Chem. Soc. 60, 863 (1938).

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# THE CHEMISTRY OF SELENOPHENE

## XII. 5-NITROSELENOPHENE-2-ALDEHYDE AND 5-NITROSELENOPHENE-2-CARBOXYLIC ACID

Iu. K. Iur'ev and E. L. Zaitseva

In a recent communication from one of us, it was shown that selenophene was formylated smoothly by dimethylformamide to form selenophene-2-aldehyde [1].

In the present work we succeeded in using N-methylformanilide for the preparation of selenophene-2-aldehyde. These two methods of formylating selenophene, which make selenophene-2-aldehyde available, allowed us to proceed to the study of its nitration, which was achieved in the present work.

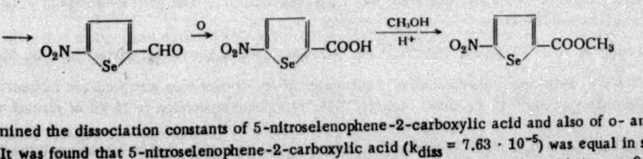
From literature data on the nitration of isologs of selenophene-2-aldehyde, it is known that Gilman and Wright [2] obtained the diacetate of 5-nitrofurfural in 33% yield by the nitration of furfural with fuming nitric acid in an acetic anhydride medium. S. A. Giller et al. [3] were able to raise the yield of the diacetate of 5-nitrofurfural to 80% by using 70% nitric acid containing 5-7% sulfuric acid for the nitration. By nitrating thiophene-2-aldehyde similarly, Zubarovskii [4] obtained the diacetate of 5-nitrothiophene-2-aldehyde in 50% yield.

As regards nitration of the selenophene nucleus, from the work of Umezawa [5], it is known that by using fuming nitric acid in acetic anhydride, he obtained 2-nitroselenophene; subsequent treatment of the 2-nitroselenophene with a mixture of nitric and sulfuric acids led to the formation of 2,4-dinitroselenophene.

We performed the nitration of selenophene-2-aldehyde in an acetic anhydride medium using fuming nitric acid (d 1.5) and obtained the diacetate of 5-nitroselenophene-2-aldehyde in 63% yield if 5-7% by weight of concentrated sulfuric acid was added to the fuming nitric acid. In the absence of sulfuric acid, the yield of the diacetate of 5-nitroselenophene-2-aldehyde fell to 28.5%.

On hydrolyzing the diacetate of 5-nitroselenophene-2-aldehyde, we obtained 5-nitroselenophene-2-aldehyde in 68% yield (43% calculated on the selenophene-2-aldehyde used in the reaction).

Oxidation of 5-nitroselenophene-2-aldehyde with potassium bichromate in sulfuric acid gave 5-nitroselenophene-2-carboxylic acid and esterification of this gave the methyl ester of 5-nitroselenophene-2-carboxylic acid.



We determined the dissociation constants of 5-nitroselenophene-2-carboxylic acid and also of o- and p-nitrobenzoic acids. It was found that 5-nitroselenophene-2-carboxylic acid ($k_{diss} = 7.63 \cdot 10^{-5}$) was equal in strength to o-nitrobenzoic acid ($k_{diss} = 4.37 \cdot 10^{-5}$) and was ten times stronger than p-nitrobenzoic acid ($k_{diss} = 9.01 \cdot 10^{-6}$).

## EXPERIMENTAL

Selenophene-2-aldehyde. Into a three-necked flask with a stirrer, a thermometer, a dropping funnel and a calcium chloride tube, was placed 20.7 g (0.137 mole) of phosphorus oxychloride and 18.5 g (0.137 mole) of N-methylformanilide, the mixture stirred and left for half an hour and then 19.65 g (0.15 mole) of selenophene added with stirring so that the temperature of the mixture remained at 23-28°. The reaction mixture was stirred at this temperature for a further 2 hours, left overnight and poured onto ice (150 g), the oily layer separated and the aqueous one extracted three times with ether. The ether extracts were combined with the oily layer and washed twice with 1.25 N hydrochloric acid. The hydrochloric acid extracts were extracted twice with ether in their turn and the either extracts added to the ether solution of the reaction product, which was then washed with sodium bicarbonate solution twice, then with water and dried over anhydrous sodium sulfate. Removal of the ether and distillation of the residue gave 17.75 g (74.5%) of selenophene-2-aldehyde.

B. p. 86-88° (7 mm), $n^{20}D$ 1.6290, $d^{20}_4$ 1.6684, $MR_D$ 33.87, $C_5H_4OSe\digamma_2$. Calculated 32.78.

Literature data: b.p. 86-87° (7 mm), $n^{20}D$ 1.6292, $d^{20}_4$ 1.6688 [1].

Diacetate of 5-nitroselenophene-2-aldehyde. Into a three-necked flask with a stirrer, a dropping funnel and a thermometer, cooled to (−5°)-(−8°), was placed 59.7 g (0.58 mole) of acetic anhydride and to it was added 19 g (0.29 mole) of fuming nitric acid (d 1.5) followed by 0.7 ml of concentrated sulfuric acid (7% of the weight of the nitric acid). The nitrating mixture was cooled to −12°, a solution of 17.4 g (0.11 mole) of selenophene-2-aldehyde in 22.9 g (0.22 mole) of acetic anhydride added to it over a period of 2 hours and the mixture stirred at this temperature for a further 4 hours, poured onto ice (450 g) and left overnight in a refrigerator. The diacetate of 5-nitroselenophene-2-aldehyde was filtered, washed with cold water and cold alcohol and dried; it had m.p. 106.5-107° (from alcohol). The crystals had a light yellow color. The yield was 20.8 g (63%).

Found %: C 35.79, 35.57; H 3.23, 3.15; N 4.45, 4.44; Se 25.31, 25.40.* $C_9H_8O_6NSe$.
Calculated %: C 35.31; H 2.97; N 4.57; Se 25.78.

Under the same reaction conditions, but in the absence of sulfuric acid, the yield of the diacetate of 5-nitroselenophene-2-aldehyde fell to 28.5%.

5-Nitroselenophene-2-aldehyde. 10 g (0.032 mole) of unpurified diacetate of 5-nitroselenophene-2-aldehyde was added to 8.3 ml of concentrated sulfuric acid in 31 ml of water and the mixture heated for 25 minutes on a boiling water bath, quickly cooled to 0° and extracted three times with ether. After evaporation of the ether, the residue was steam-distilled and the distillate obtained left overnight at 0°. The 5-nitroselenophene-2-aldehyde crystallized as long pale yellow needles with m.p. 88.5-89° (from petroleum ether). The yield was 4.6 g (68% calculated on the diacetate and 43% calculated on the selenophene-2-aldehyde used for the nitration).

Found %: C 29.50, 29.52; H 1.38, 1.36; N 6.72, 6.77; Se 38.55, 38.59. $C_5H_3O_3NSe$. Calculated %: C 29.38; H 1.48; N 6.86; Se 38.70.

The semicarbazone of 5-nitroselenophene-2-aldehyde was prepared from 0.51 g (0.0025 mole) of aldehyde, 0.28 g (0.0025 mole) of semicarbazide hydrochloride in 10 ml of water and 0.45 g of sodium acetate. The yield was 0.65 g (quantitative). The yellow crystals had m.p. 252-254° (decomp.) (from dioxane).

Found %: C 27.81, 27.64; H 2.68, 2.66; N 21.01, 21.22; Se 29.91, 29.82. $C_6H_6O_3N_4Se$. Calculated %: C 27.59; H 2.32; N 21.46; Se 30.12.

The thiosemicarbazone of 5-nitroselenophene-2-aldehyde was prepared by heating 0.51 g (0.0025 mole) of aldehyde and 0.25 g (0.0025 mole) of thiosemicarbazide in 8 ml of alcohol with 5 drops of glacial acetic acid and then adding 8 ml of water. The yield was 0.7 g (quantitative). The yellow-orange crystals had m.p. 255-257° (decomp.) (from dioxane).

Found %: C 26.09, 26.11; H 2.33, 2.40; N 20.20. $C_6H_6O_2N_4SSe$. Calculated %: C 26.00; H 2.18; N 20.21.

The 2,4-dinitrophenylhydrazone of 5-nitroselenophene-2-aldehyde was prepared by heating 0.51 g (0.0025 mole) of aldehyde and 0.45 g (0.0025 mole) of 2,4-dinitrophenylhydrazine in 10 ml of glacial acetic acid. The yield was 0.95 g (quantitative). The orange crystals had m.p. 305-307° (decomp.) (from nitrobenzene). They were insoluble in most organic solvents.

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*We are very grateful to A. S. Zabrodina for developing a convenient method for determining selenium in the analyses carried out under her direction.

Found %: N 18.00, 17.71. $C_{11}H_7O_8N_6Se$. Calculated %: N 18.23.

5-Nitroselenophene-2-carboxylic acid. 1.65 g (0.004 mole) of 5-nitroselenophene-2-aldehyde was gradually added with stirring to a solution of 1.2 g (0.002 mole) of potassium bichromate in 1.6 ml (0.015 mole) of concentrated sulfuric acid and 5 ml of water so that the temperature of the mixture did not exceed 30°. After standing for an hour, the mixture was heated for 20 minutes on a boiling water bath, cooled and extracted three times with ether and the extracts dried with anhydrous sodium sulfate. Distillation of the ether left a yellow oil, which rapidly crystallized. We obtained 1.75 g (98%) of 5-nitroselenophene-2-carboxylic acid as long yellow needles with m.p. 188.5-189° (from water).

Found %: 27.20, 27.37; H 1.60, 1.56; N 6.34, 6.34; Se 35.46, 35.58. $C_5H_3O_4NSe$. Calculated %: C 27.29; H 1.37; N 6.36; Se 35.85.

The dissociation constant of 5-nitroselenophene-2-carboxylic acid was calculated [6], as in the case of selenophene-2-carboxylic acid [7], on the basis of pH measurements on 0.01 M solutions of the acid in ethyl alcohol, 30, 50, and 70% neutralized with 0.1 N sodium hydroxide solution. The pH was measured at 20° on an LP-5 potentiometer with a glass electrode.

| Substance | $k_{diss}$ | pK |
|---|---|---|
| 5-Nitroselenophene-2-carboxylic acid | $7.63 \cdot 10^{-5}$ | 4.12 |
| o-Nitrobenzoic acid | $4.37 \cdot 10^{-5}$ | 4.36 |
| p-Nitrobenzoic acid | $9.01 \cdot 10^{-6}$ | 5.505 |

For comparison, the dissociation constants of o- and p-nitrobenzoic acids were determined under the same conditions.

The data presented show that 5-nitroselenophene-2-carboxylic acid is 10 times stronger than p-nitrobenzoic acid.

Methyl ester of 5-nitroselenophene-2-carboxylic acid. A solution of 0.55 g (0.0025 mole) of 5-nitroselenophene-2- carboxylic acid in 10 ml of anhydrous methanol was saturated with dry hydrogen chloride with cooling and kept for 18 hours. The mixture was poured into 40 ml of cold water, treated with sodium bicarbonate solution and filtered. The insoluble material – the methyl ester of 5-nitroselenophene-2-carboxylic acid – formed yellow, rose-tinted crystals with m.p. 76-76.5° (from petroleum ether). The yield was 0.42 g (73%).

Found %: C 30.62, 30,83; H 2.26, 2.44; Se 33.93, 34.03. $C_6H_5O_4NSe$. Calculated %: C 30.78; H 2.15; Se 33.76.

## SUMMARY

1. Formylation of selenophene with N-methylformanilide gave selenophene-2-aldehyde in good yield.

2. Nitration of selenophene-2-aldehyde with fuming nitric acid in the presence of a small amount of sulfuric acid yielded the diacetate of 5-nitroselenophene-2-aldehyde, which gave 5-nitroselenophene-2-aldehyde on hydrolysis. The latter was readily oxidized with potassium bichromate in sulfuric acid to form 5-nitroselenophene-2-carboxylic acid.

3. Determination of the dissociation constants of 5-nitroselenophene-2-carboxylic acid showed that it was 10 times stronger than p-nitrobenzoic acid and as strong as o-nitrobenzoic acid.

## LITERATURE CITED

[1] Iu. K. Iur'ev and N. N. Mezentseva, J. Gen. Chem. 27, 179 (1957).*

[2] H. Gilman, G. Wright, J. Am. Chem. Soc. 52, 4165 (1930).

---

*Original Russian pagination. See C.B. translation.

[3] S. A. Giller, M. M. Gershov, N. N. Naumenko and E. Iu. Gudrinietse, Auth. Cert., USSR 97012 (1952).

[4] V. M. Zubarovskii, Proc. Acad. Sci. USSR, 83, 85 (1952).

[5] S. Umezawa, Bull. Chem. Soc. Japan 11, 775 (1936).

[6] W. Kumler, J. Am. Chem. Soc. 60, 863 (1938).

[7] Iu. K. Iur'ev and N. K. Sadovaia, J. Gen. Chem. 28, 2162 (1958).

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# THE SYNTHESIS OF 2,5-DIMETHYL-3-ALKYLFURANIDINES

Iu. K. Iur'ev, E. G. Rozantsev and S. N. Godovikova

In previous papers, one of us [1] described the preparation of 3-alkylfuranidines from furanidone-3.

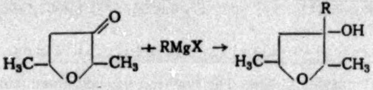
The present work is devoted to the synthesis of trialkylfuranidines with alkyl radicals in the 2,3 and 5 positions and of these, the only one described in the literature until now is 2,5-dimethyl-3-ethylfuranidine [2], which was prepared by distilling 4-ethylhexen-1-ol-5 with phosphoric acid.

We realized the synthesis of 2,3,5-trialkylfuranidines from 2,5-dimethylfuranidone-3 by the following scheme:

2,5-dimethylfuranidone-3 $\xrightarrow{AlkMgX}$ 2,5-dimethyl-3-alkyl-3-hydroxyfuranidine $\xrightarrow[I_2]{H_2O}$ 2,5-dimethyl-3-alkyldihydrofuran $\xrightarrow[Ni]{H_2}$ 2,5-dimethyl-3-alkylfuranidine.

This method of synthesizing 2,5-dimethyl-3-alkylfuranidines is more convenient as 2,5-dimethylfuranidone-3, which was first synthesized by Dupont [3], is readily obtainable by the Kucherov reaction [4] from hexyne-3-diol-2,5, which, in its turn, may be prepared by reacting acetaldehyde with Iotsich's complex.

We reacted 2,5-dimethylfuranidone-3 with alkylmagnesium halides and obtained the corresponding tertiary alcohols – 2,5-dimethyl-3-alkyl-3-hydroxyfuranidines and the maximum yield was obtained by using excess Grignard reagent and decomposing the alkoxymagnesium halide formed with ammonium acetate.

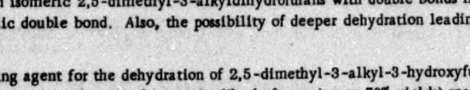


$R = CH_3, C_2H_5, C_3H_7.$

Dehydration of each of these alcohols may proceed in different directions and as a result of this the dehydration product may contain isomeric 2,5-dimethyl-3-alkyldihydrofurans with double bonds in the 2,3 and 3,4 positions and also with a semicyclic double bond. Also, the possibility of deeper dehydration leading to diene hydrocarbons, is not excluded.

The best dehydrating agent for the dehydration of 2,5-dimethyl-3-alkyl-3-hydroxyfuranidines were iodine and p-toluenesulfonic acid. The mixtures of isomeric dihydrofurans (up to 70% yields) readily polymerized on standing and on treatment with 0.1 N sulfuric acid, about 10% of the mixture dissolved, apparently indicating that this amount of the component with double bonds in the 2,3 position (a type of cyclic divinyl ether) was present [5].

After treatment of the mixture of isomeric 2,5-dimethyl-3-alkyldihydrofurans with sodium, separation of the precipitate and two distillations, a catalytic hydrogenation was performed and as a result of this we obtained the corresponding 2,5-dimethyl-3-alkylfuranidines, which were apparently mixtures of stereoisomers.



The hydrogenation was performed in the presence of Raney nickel at 20-25° at a hydrogen pressure of 60 atm. The constants and yields of the 2,5-dimethyl-3-alkylfuranidines we obtained are given in the table.

TABLE

Properties of Alkylfuranidines

| Name | Boiling point | $n^{20}D$ | $d^{20}_4$ | $MR_D$ |  | Yield (in %) |
|---|---|---|---|---|---|---|
|  |  |  |  | found | calculated |  |
| 2,3,5-Trimethylfuranidine | 112-113° (755 mm) | 1.4118 | 0.8274 | 34.33 | 33.97 | 78.0 |
| 2,5-Dimethyl-3-ethylfuranidine | 134-135 (753 mm) | 1.4241 | 0.8406 | 38.93 | 38.59 | 58.5 |
| 2,5-Dimethyl-3-propylfuranidine | 155-156 (745 mm) | 1.4300 | 0.8498 | 43.24 | 43.20 | 64.0 |

## EXPERIMENTAL

**Hexyne-3-diol-2,5.** The synthesis was performed by the procedure of Iotsich [6]. From 220 g of ethyl bromide, 48 g of magnesium and 90 g of acetaldehyde we obtained 58 g (51%) of hexyne-3-diol-2,5 with b.p. 121° (13 mm), $n^{20}D$ 1.4734, $d^{20}_4$ 1.0221.

Literature data: G. Dupont [3]: liquid isomer – b.p. 121° (15 mm), $d^{15}_0$ 1.023, $n^{15}D$ 1.4733; solid isomer – m.p. 69-70°, b.p. 122° (15 mm), $d^{15}_0$ 1.0205, $n^{15}D$ 1.4698. Zh. Iotsich [6]: b.p. 116-116.5° (9 mm), $d^{0}_0$ 1.0344, $d^{20}_0$ 1.0210. Iu.S. Zal'kind and N.G. Bessonova [7]: b.p. 169-172° (38 mm), 130-132° (22 mm), $d^{0}_4$ 1.0378, $d^{21.5}_4$ 1.02319, $n^{21.5}D$ 1.46768.

**2,5-Dimethylfuranidone-3.** The synthesis was carried out by the procedure described by Dupont [3]. From 100 g of hexyne-3-diol-2,5, 40 g of mercury sulfate and 1 ml of concentrated sulfuric acid in 300 ml of water we obtained 73 g (73%) of 2,5-dimethylfuranidone-3:

B. p. 41° (11 mm), $n^{20}D$ 1.4252, $d^{20}_4$ 0.9792, $MR_D$ 29.20. $C_6H_{10}O_2$. Calculated 29.36.

Literature data: G. Dupont [3]: b.p. 143°, $d^{15}_0$ 0.9894, $n^{15}D$ 1.4267, $MR_D$ 29.557.

### Synthesis of 2,5-dimethyl-3-alkyl-3-hydroxyfuranidines

**2,3,5-Trimethyl-3-hydroxyfuranidine.** The synthesis was performed under the usual Grignard conditions with efficient stirring and cooling of the flask with a mixture of ice and salt. From 25 g (1.05 g at.) of magnesium, gaseous methyl bromide and 100 g (0.87 mole) of 2,5-dimethylfuranidone-3 we obtained an alkoxymagnesium bromide, which was decomposed with a mixture of ice (300 g) and ammonium acetate (250 g). We obtained 118 g (90%) of 2,3,5-trimethyl-3-hydroxyfuranidine:

B. p. 173-174° (760 mm), 65.5-66° (11 mm), $n^{20}D$ 1.4423, $d^{20}_4$ 0.9720, $MR_D$ 35.46. $C_7H_{14}O_{21}$. Calculated 35.61.

Literature data [3]: b.p. 171-173° (755 mm), $n^{21}D$ 1.4420, $d^{21}_4$ 0.9719.

**2,5-Dimethyl-3-ethyl-3-hydroxyfuranidine.** The synthesis was performed under analogous conditions. From 100 g (0.87 mole) of 2,5-dimethylfuranidone-3 we obtained 110 g (88%) of 2,5-dimethyl-3-ethyl-3-hydroxyfuranidine.

b.p. 78-79° (15 mm), 181-182° (760 mm), $n^{20}D$ 1.4480, $d^{20}_4$ 0.9613, $MR_D$ 40.07, $C_8H_{16}O_2$. Calculated 40.11.

Literature data [3]: b.p. 79-81° (16 mm), $n^{21}D$ 1.4485, $d^{21}_4$ 0.9693.

**2,5-Dimethyl-3-propyl-3-hydroxyfuranidine.** From 100 g of 2,5-dimethylfuranidone-3 we obtained 110 g (80%) of 2,5-dimethyl-3-propyl-3-hydroxyfuranidine:

b.p. 191-192° (750 mm), 81.5° (8 mm), $n^{20}D$ 1.4494, $d^{20}_4$ 0.9486, $MR_D$ 44.74; calc. 44.85.

Found %: C 68.67, 68.70; H 11.49, 11.50. $C_9H_8O_2$. Calculated %: C 68.81; H 11.47.

2,5-Dimethyl-3-propyl-3-hydroxyfuranidine was an oily liquid with a musty smell; it was soluble in organic solvents and in water. It is not described in the literature.

## Preparation of 2,5-dimethyl-3-alkyldihydrofurans

2,3,5-Trimethyldihydrofuran. 10 g (0.07 mole) of 2,3,5-trimethyl-3-hydroxyfuranidine was boiled gently for 30 minutes with iodine in a flask with a fractionating column, then the liquid was slowly distilled (the temperature of the emergent vapors did not exceed 95°). The distillate was saturated with potassium carbonate and the dehydration product separated, dried with anhydrous sodium sulfate and distilled. We obtained 4.3 g (55%) of dehydration product with b.p. 100-114° (764 mm). After treatment with sodium, filtering and fractionating, the substance was a colorless, very volatile liquid with a bitter smell.

B. p. 111-112° (764 mm), $n^{20}D$ 1.4310, $d^{20}_4$ 0.850, $MR_D$ 34.16. $C_7H_{12}O$ F. Calculated 33.50.

Found %: C 75.34; 75.26; H 10.92, 10.98. $C_7H_{12}O$. Calculated %: C 74.95; H 10.78.

2,5-Dimethyl-3-ethyldihydrofuran. The dehydration was performed as described above. From 10.5 g (0.07 mole) of 2,5-dimethyl-3-ethyl-3-hydroxyfuranidine in the presence of 0.25 g of p-toluenesulfonic acid we obtained 6 g (67%) of dehydration product with b.p. 120-135° (752 mm), which had the following constants after the treatment described above:

b.p. 132-133° (755 mm), $n^{20}D$ 1.4380, $d^{20}_4$ 0.8662, $MR_D$ 38.21. $C_8H_{14}O$F. Calculated 38.12.

Found %: C 76.63, 76.84; H 11.47, 11.36. $C_8H_{14}O$. Calculated %: C 76.24; H 11.19.

2,5-Dimethyl-3-propyldihydrofuran. From 10 g of 2,5-dimethyl-3-propyl-3-hydroxyfuranidine in the presence of 0.2 g of p-toluenesulfonic acid, we obtained 5.2 g (62%) of dehydration product with b.p. 142-157° (757 mm), which had the following constants after the treatment described above:

b.p. 153-154° (750 mm), $n^{20}D$ 1.4417, $d^{20}_4$ 0.8643, $MR_D$ 42.90. $C_9H_{16}O$F. Calculated 42.73.

## Preparation of 2,5-Dimethyl-3-alkylfuranidines

2,3,5-Trimethylfuranidine. 50 g (0.44 mole) of 2,3,5-trimethyldihydrofuran was hydrogenated in a rocking autoclave in the presence of Raney nickel catalyst with a hydrogen pressure of 60 atm. After separation of the catalyst, the hydrogenation product was treated by the method described previously [1]. We obtained 39 g (78%) of 2,3,5-trimethylfuranidine:

b.p. 112-113° (755 mm), $n^{20}D$ 1.4118, $d^{20}_4$ 0.8274, $MR_D$ 34.33; calc. 33.97.

Found %: C 74.01, 73.98; H 12.40, 12.38. $C_7H_{14}O$. Calculated %: C 73.63; H 12.36.

2,3,5-Trimethylfuranidine was a very volatile liquid with a strongly bitter smell. It is not described in the literature.

2,5-Dimethyl-3-ethylfuranidine. The hydrogenation was performed as described above. From 43 g (0.37 mole) of 2,5-dimethyl-3-ethyldihydrofuran we obtained 28 g (58.5%) of 2,5-dimethyl-3-ethylfuranidine:

b.p. 134-135° (750 mm), $n^{20}D$ 1.4241, $d^{20}_4$ 0.8406, $MR_D$ 38.93. $C_8H_{16}O$. Calculated 38.59.

Literature data [2]: b.p. 134° (754 mm), $n^{18}D$ 1.4238, $d^{18}_4$ 0.843.

2,5-Dimethyl-3-propylfuranidine. The hydrogenation was performed as described above. From 97 g of 2,5-dimethyl-3-propyldihyrofuran we obtained 51.2 g (69%) of 2,5-dimethyl-3-propylfuranidine:

B. p. 155.5-156° (745 mm), $n^{20}D$ 1.4300, $d^{20}_4$ 0.8438, $MR_D$ 43.24, calc. 43.20.

Found %: C 76.01, 75.98; H 12.42, 12.60. $C_9H_{18}O$. Calculated %: C 76.02; H 12.76.

2,5-Dimethyl-3-propylfuranidine was a mobile, volatile liquid with a bitter smell. It is not described in the literature.

## SUMMARY

Organomagnesium synthesis of 2,5-dimethyl-3-alkyl-3-hydroxyfuranidines from 2,5-dimethylfuranidone-3 is a convenient way of synthesizing tertiary alcohols of the furanidine series. By this method we prepared 2,3,5-trimethyl-3-hydroxyfuranidine, 2,5-dimethyl-3-ethyl-3-hydroxyfuranidine and 2,5-dimethyl-3-propyl-3-hydroxyfuranidine, of which the latter is not described in the literature.

Dehydration of the 2,5-dimethyl-3-alkyl-3-hydroxyfuranidines led to a mixture of isomeric dihyrofurans with traces of diene hydrocarbons. The best dehydrating agents for the dehydration of tertiary alcohols of the furanidine series were iodine and p-toluenesulfonic acid.

Catalytic hydrogenation of the 2,5-dimethyl-3-alkyldihydrofurans led to the formation of 2,5-dimethyl-3-alkylfuranidines.

The synthesis of 2,3,5-trialkylfuranidines from 2,5-dimethylfuranidone-3, described in the present work, is a general method of synthesizing furanidine homologs of this structure.

## LITERATURE CITED

[1] Iu. K. Iur'ev, E. M. Lukina, Iu. M. Polikarpov and V. P. Volkov, J. Gen. Chem. 26, 553 (1956);* Iu. K. Iur'ev, E. M. Lukina and I. K. Korobitsyna, J. Gen. Chem. 24, 1248 (1954).*

[2] G. Colonge et A. A. Zagier, C. r. 224, 572 (1947).

[3] G. Dupont, Ann. Chim. [8], 30, 501 (1913).

[4] M. G. Kucherov, J. Russ. Chem. Soc. 13, 542 (1881); Ber. 14, 1540 (1881); Ber. 17, 13 (1884); Ber. 42, 2759 (1909).

[5] R. Paul et H. Normant, Bull. Soc. Chim. [5] 11, 365 (1944).

[6] Zh. N. Iotsich, J. Russ. Chem. Soc. 35, 430 (1903).

[7] Iu. S. Zal'kind and I. G. Bessonova, J. Russ. Chem. Soc. 53, 279 (1921).

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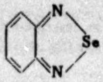
# SOME AMINO DERIVATIVES OF PIAZSELENOLE

L. S. Efros and A. V. El'tsev

In previous communications [1, 2] it was shown that piazselenole has quinoid structure (I). In particular, this is indicated by data from interatomic distance measurements, presented by Luzzati [3].

As was observed recently [2], 5-aminopiazselenole (II) is capable of undergoing azo coupling and structure (III) was proposed for the azo compound obtained from structure (I).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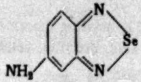
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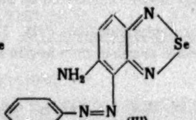
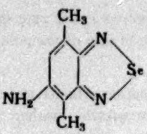

(III)

The possibilities of determining the position of the azo group directly in this case are very limited as, firstly, reducing agents very readily destroy the selenodiazole ring and, secondly, amino derivatives of piazselenole are quite sensitive to atmospheric oxygen.

To prove the proposed direction of the azo coupling reaction of 5-aminopiazselenole, we synthesized amines (IV) and (V), in one of which positions 4 and 7 and in the other, 6, are blocked with methyl groups. Both of the amines were prepared by mixing aqueous solutions of the appropriate substituted triaminobenzene hydrochlorides and sodium selenite. In addition we also characterized the nitro compounds (VI) and (VII), which were readily formed from the appropriate ortho diamines and selenium dioxide.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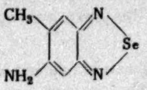
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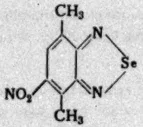
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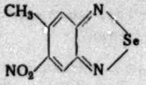
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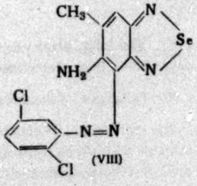
(VIII)

The 1,2,4-triamino-3,6-dimethylbenzene, required for the synthesis of substance (IV) has not been described in the literature previously; we prepared it by the reduction of trinitro-p-xylene with tin in hydrochloric acid. We were unable to identify the triamine directly; the most convenient way was the very simple preparation of 5-amino-4,7-dimethylpiazselenole (IV) from it.

It was found that 5-amino-6-methylpiazselenole (V) very readily underwent azo coupling with aryldiazonium salts. We characterized the azo dye (VIII), prepared from (V) and diazotized 2,5-dichloroaniline. In the case of 5-amino-4,7-dimethylpiazselenole (IV), as would be expected, all attempts to perform an azo coupling reaction were unsuccessful, and the most active of the diazo components tried – diazotized p-nitroaniline – formed only a diazoamino compound. Steric hindrance, caused by the two methyl groups, apparently, is not of decisive importance here, as in the case of 5-hydroxy-4,7-dimethylhydrindene [4] and 5-amino-4,7-dimethylbenzimidazolone [5] the azo coupling reaction proceeds smoothly.

The facts presented leave hardly any doubt as regards the accuracy of the structure proposed for the azo dye (IV) and support the quinoid structure of piazselenole (I) with augmentation of the double bond character between carbon atoms 5-4 and 6-7.

## EXPERIMENTAL

The nitro compounds were prepared by mixing aqueous acetone solutions of the appropriate nitro-o-diamines and selenious acid. The precipitate of the nitro product formed was filtered off and recrystallized from a suitable solvent. The yield was 60-70°, calculated on the pure substance.

5-Nitro-4,7-dimethylpiazselenole (VI). The starting diamine was described previously [5]. After recrystallization from ethyl acetate and then from acetic acid, the fine, yellow needles of 5-nitro-4,7-dimethylpiazselenole melted at 197-198°.

Found %: N 16.56, 16.65. $C_8H_7O_2N_3$. Calculated %: N 16.41.

5-Nitro-6-methylpiazselenole (VII). The starting product was a mixture of amines, obtained by partial reduction of 2,4-dinitro-5-methylaniline [6]. After two recrystallizations from ethyl acetate, the slightly yellowish needles of 5-nitro-6-methylpiazselenole melted at 165-166°.

Found %: N 17.34, 17.54. $C_7H_5O_2N_3$. Calculated %: N 17.36.

1,2,4-Triamino-3,6-dimethylbenzene. 6 g of trinitro-p-xylene was reduced with 21 g of tin in 60 ml of concentrated hydrochloric acid; the tin was precipitated from a highly dilute solution (600 ml) with hydrogen sulfide and filtered off. The filtrate was evaporated in vacuum and the triamine hydrochloride obtained was used for the synthesis of 5-amino-4,7-dimethylpiazselenole without additional purification.

The triamine base was readily soluble in water and rapidly oxidized in air. The sulfate, chloride, bromide and fluoborate were readily soluble in water and in the corresponding strong acids.

The 2-nitroindanedione-1,3-ate of the triamine could not be recrystallized, as it was very sparingly soluble and darkened and decomposed when heated with water. The picrate and styphnate also decomposed on heating with dilute alcohol.

The amino compounds were synthesized by mixing aqueous solutions of sodium selenite and the hydrochloride of the appropriate triamine. The amine bases were quickly filtered off from the solution, washed with alcohol on the filter and recrystallized from a convenient solvent without preliminary drying. The yield was 45-50%, calculated on the pure product.

5-Amino-4,7-dimethylpiazselenole (IV). The long, clear yellow needles (from chlorobenzene with charcoal added) melted at 211°. The hydrochloride had a dark claret color and was difficultly soluble in water.

Found %: C 42.37, 42.19; H 4.02, 4.06. $C_8H_9N_3Se$. Calculated %: C 42.48; H 4.01.

5-Amino-6-methylpiazselenole (V). The starting 1,2,4-triamino-5-methylbenzene hydrochloride [7] was prepared by reducing 2,4-dinitro-5-methylaniline with tin in hydrochloric acid. After recrystallization from chlorobenzene and then from chloroform, the 5-methyl-6-aminopiazselenole formed coarse yellow needles melting at 187°. The hydrochloride of the amine was red and difficultly soluble in water.

Found %: C 39.88, 39.63; H 3.43, 3.37. $C_7H_7N_3Se$. Calculated %: C 39.64; H 3.33.

5-Amino-6-methyl-4-(2',5'-dichlorophenylazo)-piazselenole (VIII). A solution of 0.5 g of 2,5-dichlorophenyldiazonium fluoborate in 30 ml of water was poured with stirring into a solution of 0.4 g of 5-methyl-6-aminopiazselenole in 50 ml of water (with the minimum amount of hydrochloric acid added to completely dissolve the amine). After 5 minutes, the hydrochloride of the azo dye was filtered off and washed on the filter with sodium acetate solution and water. After recrystallization from a large volume of chloroform, the light red needles of the dye base melted from a large volume of chloroform, the light red needles of the dye base melted at 258°.

Found %: C 40.68, 40.27; H 2.28, 2.75. $C_{13}H_9N_5SeCl_2$. Calculated %: C 40.54; H 2.36.

## SUMMARY

In order to elucidate the direction of the azo coupling reaction of 5-aminopiazselenole, a study was made of the reactions of 5-amino-6-methylpiazselenole and 5-amino-4,7-dimethylpiazselenole with diazonium salts. The inability of the latter to form an azo compound, supports the proposal that the azo group is attached to the fourth carbon atom in 5-aminopiazselenole.

## LITERATURE CITED

[1] L. S. Efros, Z. V. Todres-Selektor, J. Gen. Chem. 27, 983 (1957).*

[2] L. S. Efros, Z. V. Todres-Selektor, J. Gen. Chem. 27, 3127 (1957).*

[3] V. Luzzati, Acta Cryst. 4, 193 (1951).

[4] L. Fieser and W. Lothrop, J. Am. Chem. Soc. 58, 2050 (1936).

[5] L. S. Efros, A. V. El'tsov, J.Gen. Chem. 28, 941 (1958).*

[6] L. S. Efros, A. V. El'tsov, J. Gen. Chem. 28, 62 (1958).*

[7] Ruhemann, Ber. 14, 2657 (1881).

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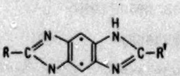
# INVESTIGATION IN THE FIELD OF IMIDAZOLE DERIVATIVES

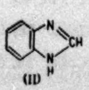
## XXI. SYNTHESIS AND PROPERTIES OF IMIDAZOLONOIMIDAZOLOBENZENES

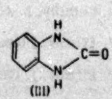
L. S. Efros and A. V. El'tsov

The diimidazolobenzenes (I) studied previously were close in their chemical properties to anthracene derivatives [1]: when oxidized with chromic mixture, they formed quinones and when halogenated, dihalogen derivatives and nitration led to the formation of mononitro compounds.

This behavior of compound (I) is caused by the effect of the aromatic imidazole rings on the central benzene nucleus, the meso position of which becomes radically unsaturated. As we proposed [2, 3], in contrast to benzimidazole (II), the electron cloud of benzimidazole is deformed in such a way that the double bond character between carbon atoms 5 and 6 is increased (III).

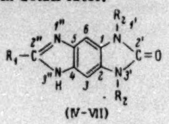

(I)

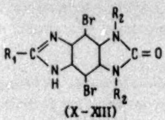

(II)

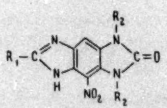

(III)

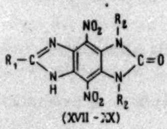
Therefore, it seemed interesting to us to study the properties of a compound in which the benzene ring was condensed both with an imidazole and an imidazolone heterocycle. One would imagine that in comparison with compound (I), such a molecule would have considerably less radical unsaturation of the meso position, a higher reactivity in substitution reactions and a lower stability of the benzene nucleus due to a decrease in its aromatic properties.

By treating 5,6-diaminobenzimidazolone and its 1,3-dimethyl analog with formic and acetic acids, we synthesized compounds (IV) [4], (V) [5] and (VI), (VII) respectively. When fused with urea, the starting diamines readily formed substances (VIII) and (IX), which have not been described in the literature previously and whose properties we propose to study in detail later.

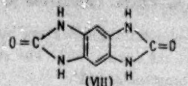

(IV–VII)

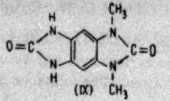

(X–XIII)


(XV–XVI)


(XVII–XX)

(IV, X, XV, XVII) $R_1 = R_2 = H$;
(V, XI, XV, XVIII) $R_1 = CH_3$, $R_2 = H$;
(VI, XII, XVI, XIX) $R_1 = H$, $R_2 = CH_3$;
(VII, XIII, XX) $R_1 = R_2 = CH_3$.


(VIII)


(IX)

It was found that chromic mixture had a destructive effect on compounds (IV) – (VII); we were unable to isolate quinones, even when the reaction was performed at 0°. Bromination of the compounds studied proceeded very readily and gave the dibromides (X) – (XIII). The mononitro compounds (XIV) – (XVI) were isolated by nitration of the 1,2-imidazolone-4,5-imidazolobenzenes (IV) – (VII) with the theoretical amount of nitrating mixture at 0°. At higher temperatures (20°) and with excess nitrating mixture, we obtained the dinitro compounds (XVII) – – (XX). We should note that attempts to introduce two nitro groups into 1,2,4,5-dimidazolobenzene (I) was not successful [1]. The dinitro products (XVII) and (XVIII) were very sparingly soluble and therefore we were unable to purify them sufficiently well and to determine their elementary compositions with the required accuracy. However, elementary analysis data obtained for these substances made it possible to find the empirical formula from the ratio of the elements and this corresponded to the proposed structure.

Thus, the experimental facts presented confirm our hypotheses on the possible results of the simultaneous effect of an imidazolone and an imidazole ring on a benzene ring condensed with them. To a certain extent, this may serve as further proof of our conclusions on the deformation of the electron cloud of the benzene nucleus under the effect of the imidazolone ring.

## EXPERIMENTAL

1,2-(1',3'-Dimethyl)-imidazolono-4,5-imidazolobenzene (VI). 9 g of 5,6-diamino-1,3-dimethylbenzimidazolone dihydrochloride [2] was heated for 2 hours with 50 ml of 99% formic acid in a flask with a reflux condenser. Then the contents of the flask were poured into a porcelain dish and evaporated to dryness on a water bath. The dry residue was dissolved in 100 ml of boiling water and the solution treated with animal charcoal and, after cooling, neutralized with ammonia. The precipitate formed was filtered off and recrystallized from water. Drying at 105° yielded 6 g of pure product in the form of a colorless powder, melting at 276°.

Found %: N 27.96, 27.80. $C_{10}H_{10}ON_4$. Calculated %: N 27.71.

1,2-(1',3'-Dimethyl)-imidazolono-4,5-(2''-methyl)-imidazolobenzene (VII) was synthesized similarly to the compound described above, except that the formic acid was replaced by excess acetic anhydride. Recrystallization from alcohol and drying at 105° gave a 65% yield of a colorless powder, which did not melt at 320°.

Found %: N 26.14, 26.00. $C_{11}H_{12}ON_4$. Calculated %: N 25.91.

1,2,4,5-(1',3'-Dimethyl)-diimidazolonobenzene (IX). 7.8 g of 5,6-diamino-1,3-dimethylbenzimidazolone dihydrochloride was ground in a mortar with 7 g of urea and the mixture placed in a crucible and heated on an oil bath. At 170° the mixture rapidly solidified. The solidified melt was cooled and dissolved in hot 8% alkali (400 ml) and the solution treated with animal charcoal and acidified with hydrochloric acid. The precipitate was recrystallized from acetic acid and dried at 105°. We obtained 5 g of a substance as a colorless, amorphous powder, which was sparingly soluble in organic solvents and did not melt at 320°.

Found %: C 55.11, 54.82; H 4.72, 4.71. $C_{10}H_{10}O_2N_4$. Calculated %: C 55.05; H 4.62.

1,2,4,5-Diimidazolonobenzene (VIII) was synthesized similarly to the previous substance, except that the starting product used was 10 g of 5,6-diaminobenzimidazolone dihydrochloride. We obtained 7.5 g of a greyish, amorphous powder, which was sparingly soluble in organic solvents and did not melt at 320°. For analysis, the product was reprecipitated several times from alkali with acid and washed on the filter with water and acetone.

Found %: C 50.26; H 3.17; N 29.48, 29.55. $C_8H_6O_2N_4$. Calculated %: C 50.53; H 3.18; N 29.46.

Bromination of 1,2-imidazolono-4,5-imidazolobenzene derivatives was achieved by adding excess bromine to a solution of 0.5 g of the dihydrochloride of the starting material in 20 ml of warm water. The dibromide was precipitated from the solution with ammonia or excess hydrochloric acid and purified.

3,6-Dibromo-1,2-imidazolono-4,5-imidazolobenzene hydrochloride (X). The substance was recrystallized several times from hydrochloric acid and dried at 60°. The snow-white needles did not melt at 320°.

Found %: C 25.96; H 1.68; N 15.18. $C_8H_{11}ON_4Br_2 \cdot HCl$. Calculated %: C 26.08; H 1.37; N 15.21.

3,6-Dibromo-1,2-(1',3'-dimethyl)-imidazolono-4,5-imidazolobenzene hydrochloride (XII). The substance was recrystallized several times from hydrochloric acid and dried at 60°. The very small, snow-white needles contained water of crystallization. The substance decomposed at 311°.

Found %: C 28.87, 28.96; H 2.81, 2.73. $C_{10}H_8ON_4Br_2 \cdot H_2O$. Calculated %: C 28.97; H 2.67.

3,6-Dibromo-1,2-imidazolono-4,5-(2"-methyl)-imidazolobenzene (XI). The dibromide base was recrystallized from aqueous alcohol. The colorless needles obtained contained water of crystallization, which was readily removed by drying. The hygroscopic, amorphous powder did not melt at 320°.

Found %: N 16.11, 16.03. $C_9H_6ON_4Br_2$. Calculated %: N 16.19.

3,6-Dibromo-1,2-(1',3'-dimethyl)-imidazolono-4,5-(2"-methyl)-imidazolobenzene (XIII). The base was recrystallized from aqueous alcohol. The colorless, amorphous powder did not melt at 320°.

Found %: C 35.03, 35.51; H 2.79, 2.65. $C_{11}H_{10}ON_4Br_2$. Calculated %: C 35.32; H 2.69.

The mononitro derivatives were prepared in the following way. 1 g of the starting material (in the form of the base) was dissolved in 10 ml of concentrated sufluric acid (d 1.83), the solution was cooled to −5° and to it was added dropwise a nitrating mixture from 2 ml of $H_2SO_4$ (d 1.83) and the calculated amount of concentrated nitric acid (d 1.513). After a little stirring, the reaction mixture was poured onto ice and the mononitro compound separated from the solution and purified.

3-Nitro-1,2-imidazolono-4,5-imidazolobenzene sulfate (XIV). When the reaction mixture from the nitration was poured onto ice, a yellow precipitate of the mononitro-derivative sulfate formed and this was recrystallized several times from dilute sulfuric acid, washed on the filter with anhydrous alcohol and ether and dried at 80°. The yellow crystals were sparingly soluble in water.

Found %: S 10.32, 10.15; N 22.35. $C_8H_5O_3N_5 \cdot H_2SO_4$. Calculated %: S 10.11; N 22.08.

3-Nitro-1,2-imidazolono-4,5-(2"-methyl)-imidazolobenzene hydrochloride (XV). The reaction mixture from the nitration was poured onto ice, neutralized with ammonia and the precipitate which formed recrystallized several times from dilute hydrochloric acid. The yellow needles were quite readily soluble in water.

Found %: C 40.07; H 2.98. $C_9H_7O_3N_5 \cdot HCl$. Calculated %: C 40.09; H 2.99.

3-Nitro-1,2-(1',3'-dimethyl)-imidazolono-4,5-imidazolobenzene (XVI). The reaction mixture from nitration was poured onto ice and neturalized with ammonia and the precipitate filtered and recrystallized from glacial acetic acid and then from pyridine; the orange-yellow needles did not melt at 320°.

Found %: C 48.53; H 3.60; $C_{10}H_9O_3N_5$. Calculated %: C 48.58; H 3.70.

The dinitro derivatives were prepared in the same way as the mononitro derivatives with the only difference that excess nitric acid was used for the nitration and the reaction was performed at 20°. After the addition of the nitrating mixture, the reaction mass was stirred for 1 hour, then poured onto ice and neutralized with ammonia and the precipitate of dinitro product purified.

3,6-Dinitro-1,2-(1',3'-dimethyl)-imidazolono-4,5-imidazolobenzene (XIX). The yellow crystals (from chlorobenzene) melted at 287°.

Found %: C 41.03, 41.21; H 2.85, 2.95. $C_{10}H_8O_5N_6$. Calculated %: C 41.10; H 2.76.

3,6-Dinitro-1,2-(1',3'-dimethyl)-imidazolono-4,5-(2"-methyl)-imidazolobenzene (XX). The fine orange needles (from aqueous pyridine) melted at 284°.

Found %: C 43.02, 43.19; H 3.07, 3.28. $C_{11}H_{10}O_5N_6$. Calculated %: C 43.14; H 3.29.

3,6-Dinitro-1,2-imidazolono-4,5-imidazolobenzene (XVII). The dark-red amorphous powder was washed on the filter with distilled water, then acetone, alcohol and ether. The substance did not melt at 320°.

Found %: C 34.05, 34.19, 33.84; H 2.39, 2.37, 2.51; N 28.88, 28.82.* $C_8H_4O_5N_6$. Calculated %: C 36.37; H 1.53; N 31.82.

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* These analysis data give the formula $C_8H_{6.8}O_{6.1}N_{5.8}$.

**3,6-Dinitro-1,2-imidazolono-4,5-(2"-methyl)-imidazolobenzene (XVIII).** The red, amorphous powder was washed on the filter with distilled water, then acetone, alcohol and ether. The substance did not melt at 320°.

Found %: C 37.05, 37.02, 37.00; H 3.17, 3.24, 3.02; N 29.55, 29.27.* $C_9H_6O_5N_6$. Calculated %: C38.86; H 2.17; N 30.21.

## SUMMARY

A study was made of the oxidation, bromination and nitration reactions of 1,2-imidazolono-4,5-imidazolobenzene derivatives and it was established that they have a higher reactivity than 1,2,4,5-diimidazolobenzene derivatives.

## LITERATURE CITED

[1] L. S. Efros, J. Gen. Chem. 22, 1015 (1952).*

[2] L. S. Efros and A. V. El'tsov, J. Gen. Chem. 28, 441 (1958).*

[3] L. S. Efros and A. V. El'tsov, J. Gen. Chem. 28, 941 (1958).*

[4] A. T. James and E. E. Turher, J. Chem. Soc. 1950, 1515.

[5] O. Kym and L. Ratner, Ber. 45, 3245 (1912).

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* These analysis data give the formula $C_9H_9O_{5.5}N_{6.1}$.

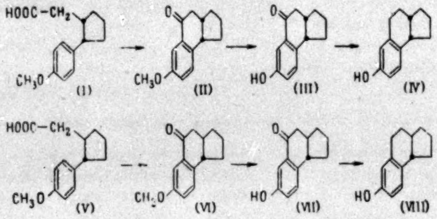
** Original Russian pagination. See C.B. translation.

# INVESTIGATION IN THE FIELD OF THE SYNTHESIS OF STEROID HORMONE ANALOGS

## V. THE SYNTHESIS OF SOME COMPOUNDS OF THE CYCLOPENTANOTETRAHYDRONAPHTHALENE SERIES

V. I. Maksimov and G. S. Grinenko

In the course of investigations on the synthesis of steroid hormone analogs, we obtained tricyclic compounds, containing rings B, C, and D of the steroid nucleus. Cis- and trans-4-keto-6-methoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalenes (II) and (VI) were formed by the intramolecular acylation of the cis- and trans-isomers of 2-(p-methoxyphenyl)-cyclopentane-1-acetic acid (I, V), respectively [1].



The cyclization was performed by three methods: by the action of polyphosphoric acid, or hydrogen fluoride* and by the Friedel – Crafts method, using stannic chloride as the condensing agent. In all cases the cis-acid (I) gave an almost quantitative yield of the cis-tricyclic ketone (II) and the trans-acid (V) gave only a 70% yield of the trans-tricyclic ketone under the same conditions. The greater tendency of the cis-acid (I) towards cyclization in comparison with the trans-acid (V) is explained by the lower strain in cis-hydrindan [2].

The cis-tricyclic ketone (II) and its semicarbazone have lower melting points and higher solubilities than the corresponding compounds of the trans series. This agrees with the rule that, in general, the trans-isomer melts at a higher temperature and is less soluble [2, 3]. The same rule governs the physical constants of compounds (III), (IV), (VII), and (VIII) and their derivatives, prepared from the corresponding ketones (II) and (VI).

Thus, the difference in tendency towards cyclization of the cis- and trans-acids (I) and (V) and the physical constants and solubilities of the tricyclic compounds obtained from them confirm the accuracy of the configurations proposed for them [1].

## EXPERIMENTAL

Cis-4-keto-6-methoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene (II). a) Cyclization by the Friedel – Crafts method. To a solution of 1.37 g (0.0059 mole) of cis-2-(p-methoxyphenyl)-cyclopentane-1-

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* We are very grateful to V. F. Sukhoverkhov for helping to carry out the cyclization under the action of hydrogen fluoride.

acetic acid (I) in 30 ml of anhydrous benzene was added 8.5 g (0.04 mole) of finely powdered phosphorus pentachloride. After being stirred at room temperature for half an hour, the reaction mixture was cooled with ice-water and a solution of 7 ml (0.04 mole) of stannic chloride in 15 ml of anhydrous benzene was added dropwise. The reaction mixture was stirred for 1 hour at room temperature and then decomposed with ice and dilute hydrochloric acid. The benzene layer was separated and the aqueous one extracted with ether. The benzene ether extract was washed with 5% alkali solution first and then with water and dried. The residue after evaporation of the solvent was a dark-colored, mobile oil, which was either vacuum-distilled (b.p. 136-138° at 0.35 mm) or passed through a column with 20 g of aluminum oxide in benzine (the tars remained as a narrow ring in the upper part of the column). In both cases we obtained 1.14 g of cis-4-keto-6-methoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene in the form of a colorless oil, which rapidly crystallized (m.p. 27-29°, $\lambda_{max}$ 250 mμ, log ε 3.818). The yield was 90%.

Found %: C 77.82; H 7.57. $C_{14}H_{16}O_2$. Calculated %: C 77.75; H. 7.44.

The semicarbazone of cis-4-keto-6-methoxy-1,2-cyclopentano-1,2,3,4-tetrahydropaphthalene had m.p. 169-170° (from alcohol).

Found %: C 65.74; H 6.94; N 15.04. $C_{15}H_{19}O_2N_3$. Calculated %: C 65.91; H 6.97; N 15.37.

b) Under the action of hydrogen fluoride. Into a ftorplast* vessel was placed 3 g of cis-2-(p-methoxyphenyl)-cyclopentane-1-acetic acid and approximately 35 g of liquid hydrogen fluoride. The reaction mixture was allowed to stand for 2 hours, after which the hydrogen fluoride was removed in a stream of air and the residue dissolved in chloroform. The chloroform solution was washed with 5% soda solution and water and dried. The residue, after evaporation of the chloroform, was an almost colorless oil, which was treated by the method described above. An almost quantitative yield of cis-4-keto-6-methoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene was obtained.

Cis-4-keto-6-hydroxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene (III). A solution of 2 g (0.0093 mole) of cis-4-keto-6-methoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene (II) in 40 ml of glacial acetic acid and 40 ml of hydrobromic acid was boiled for 2.5 hours in a stream of nitrogen. The residue after evaporation of the acetic acid was dissolved in 5% sodium hydroxide solution and extracted with ether. The alkaline solution was acidified. The oil which separated was washed with water, dried and decolorized by shaking with activated charcoal. After distilling off the ether, we obtained 1.45 g of cis-4-keto-6-hydroxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene in the form of clusters of needles. Two recrystallizations from benzene yielded 1.3 g (69.5%) of products with m.p. 111-112°.

Found %: C 77.45; H 6.83. $C_{13}H_{14}O_2$. Calculated %: C 77.20; H 6.98.

Cis-6-hydroxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene (IV). A solution of 0.2 g of cis-6-hydroxy-4-keto-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene (III) in 2.5 ml of diethylene glycol and 0.16 ml of hydrazine hydrate was boiled for 2 hours. Then 0.25 g of sodium hydroxide was added and the mixture heated at 190-195° for 3 hours. After cooling, the reaction mixture was poured into 5 ml of water and acidified with 5% hydrochloric acid. The oil liberated was extracted with ether. The ether extract was washed with water, dried and evaporated down. We obtained 0.16 g of cis-6-hydroxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene with m.p. 66-67° (from a mixture of ether and petroleum ether).

Found %: C 82.84; H 8.52. $C_{13}H_{16}O$. Calculated %: C 82.93; H 8.57.

Cis-6-benzoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene. To a solution of 0.46 g of the cis-phenol (IV) in 20 ml of 10% sodium hydroxide was added 3 ml of benzoyl chloride and the mixture shaken until the smell of benzoyl chloride disappeared (3-4 hours). The oil produced was extracted with ether. The ether extract was washed with water until neutral and dried. The residue after evaporation of the ether (0.7 g) was passed through a column containing 7 g of aluminum oxide in carbon tetrachloride solution. We obtained 0.65 g of cis-6-benzoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene with m.p. 81-82° (from a mixture of equal parts of alcohol and ether).

Found %: C 82.03; H 6.93. $C_{20}H_{20}O_2$. Calculated %: C 82.16; H 6.89.

Trans-4-keto-6-methoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene (VI). a) Under the action of hydrogen fluoride. 3.5 g of trans-2-(p-methoxyphenyl)-cyclopentane-1-acetic acid (V) was cyclized with 10 times the amount of hydrogen fluoride, as described above. As a result of working up in a similar way, we obtained 2.2 g (68.1%) of trans-4-keto-6-methoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene in the form of needles with m.p. 95.5-96.5° (from alcohol) ($\lambda_{max}$ 250 mμ, log ε 3.8).

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*As in Russian, polytetrafluoroethylene or a derivative – Publisher's note.

Found %: C 77.47; H 7.51. $C_{14}H_{16}O_2$. Calculated %: C 77.75; H 7.44.

The semicarbazone of trans-4-keto-6-methoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene was almost insoluble in alcohol and had m.p. 245° (with decomp.).

Found %: N 15.11. $C_{15}H_{19}O_2N_3$. Calculated %: N 15.37.

b) Under the action of polyphosphoric acid. The polyphosphoric acid was prepared by Uhling's method [4] from 80 ml of sirupy phosphoric acid (d 1.75), to which 120 g of phosphorus pentoxide was gradually added with stirring and cooling. The polyphosphoric acid prepared in this way was an almost colorless liquid, which was immobile at room temperature, but quite mobile at 50-60°. The polyphosphoric acid was heated to 80°, 10 g of trans-2-(p-methoxyphenyl)-cyclopentane-1-acetic acid added and the mixture stirred for 3-4 minutes. The acid dissolved completely and the reaction mixture acquired a red color. The reaction mixture was poured onto ice. The greenish-yellow tarry precipitate formed was extracted with ether. The ether extract was washed first with water, then with 5% soda solution and again with water until neutral and dried over anhydrous sodium sulfate. After distilling off the ether, we obtained 7.25 g of trans-4-keto-6-methoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene in the form of small yellow needles. Recrystallization from alcohol did not remove the yellow color of the precipitate and only after a benzene solution of the latter had been passed through a small layer of aluminum oxide was the color retained as a narrow ring in the column and 6.6 g (71.9%) of the colorless substance with m.p. 95.5-96.5° was obtained.

Trans-4-keto-6-hydroxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene (VII). 0.4 g of trans-4-keto-6-methoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene (VI) was demethylated in a solution of 8 ml of glacial acetic acid and 8 ml of hydrobromic acid under the conditions described for the cis-isomer. After working up appropriately, we obtained 0.35 g of trans-4-keto-6-hydroxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene in the form of small needles with m.p. 193-193.5° (from benzene).

Found %: C 77.40; H 6.98. $C_{13}H_{14}O_2$. Calculated %: C 77.20; H 6.98.

Trans-6-hydroxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene (VIII). 0.25 g of the trans-6-hydroxy-4-keto-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene (VII) was reduced by the Kishner method. as described for the cis-isomer. We obtained 0.21 g of trans-6-hydroxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene with m.p. 76-76.5° (from a mixture of benzine and benzene).

Found %: C 83.15; H 8.52. $C_{13}H_{16}O$. Calculated %: C 82.93; H 8.57.

Trans-6-benzoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene. The phenolate obtained from 0.14 g of trans-6-hydroxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene and 6 ml of 10% sodium hydroxide, was shaken with 1 ml of benzoyl chloride. The reaction mixture was extracted with ether. The ether extract was washed with water and dried over anhydrous sodium sulfate. The residue from evaporation of the ether was recrystallized from a 40-fold amount of alcohol. We obtained 0.2 g of trans-6-benzoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene with m.p. 93.8-94.3°.

Found %: C 81.97; H 7.01. $C_{20}H_{20}O_2$. Calculated %: C 82.16; H 6.89.

## SUMMARY

1. Preparations are described for the stereoisomeric cis- and trans-forms of 4-keto-6-methoxy-1,2-cyclopentano-1,2,3,4-tetrahydronaphthalene by the intramolecular acylation of the corresponding cis- and trans-2-(p-methoxyphenyl)-cyclopentane-1-acetic acids.

2. The configurations of these acids were confirmed by the difference in their tendencies towards cyclization.

## LITERATURE CITED

[1] G. S. Grinenko, V. I. Maksimov, J. Gen. Chem. 28, 532 (1958).*

[2] W. Hückel, M. Sachs, J. Vantschulewitsch and F. Nerdel, Lieb. Ann. 518, 155 (1935).

---

*Original Russian pagination. See C.B. translation.

[3] W. Hückel, Lieb. Ann. 441, 1 (1925).

[4] F. Uhlig, Ang. Chem. 66, 435 (1954).

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# INVESTIGATION IN THE FIELD OF THE SYNTHESIS OF STEROID HORMONE ANALOGS

## VI. EXPERIMENTS ON THE CYCLIZATION OF TRANS-3-(p-METHOXYPHENYL)-CYCLOPENTAN-1-ONE-2-ACETIC ACID AND ITS DERIVATIVES

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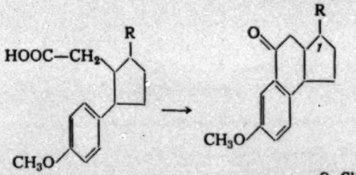
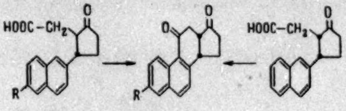
In a previous paper [1] we showed that cis- and trans- tricyclic ketones of type (II) (R= H) could be prepared by intramolecular acylation of phenylcyclopentylacetic acids of type (I) (R= H).



(I) R = H

(II) R = H (III) R = $<\begin{matrix}O-CH_2\\ |\\ O-CH_2\end{matrix}$,
(IV) R = O, (V) R = $OCOCH_3$.

The synthesis of R. Robinson [2], which was an unsuccessful attempt to synthesize equilenine by intramolecular acylation of 3-(β-methoxynaphthyl)-cyclopentan-1-one-2-acetic acid (VI), lead to the stereoisomeric D,L-isoequilenine. The presence of the carboxyl group at a position adjacent to the asymmetric carbon atom facilitated the conversion (through an enolization stage) to the stable cis-α-hydrindanone (VIII) [3].



(VI) R = $OCH_3$
(VII) R = H

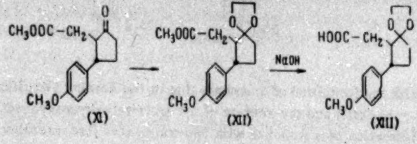
(VIII) R = $OCH_3$
(IX) R = H

(X)

This conversion was observed by Weidlich [4], when on cyclizing both the cis- (X) and the trans-3-(β-naphthyl)-cyclopentan-1-one-2-acetic acids (VII), he obtained the same tetracyclic diketone (IX).

To obtain a trans configuration of the ring in the tricyclic ketone (IV) during the cyclization of the trans-ketoacid (XVI), it is necessary to convert the carbonyl group of this acid into another group, which excludes the possibility of epimerization of the adjacent asymmetric carbon atom.

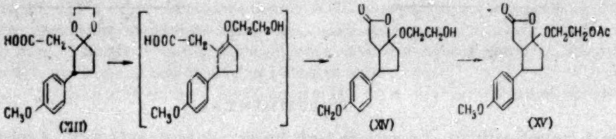
For this purpose, we performed the cyclization of the ethyleneketal of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid (XIII) and anti-trans-3-(p-methoxyphenyl)-cyclopentane-1-acetoxy-2-acetic acid (XVIII). We prepared the ethyleneketal of the trans-ketoacid (XIII) (according to the method proposed by Wieland, Anner and Miescher [5] for ketoacids) by alkaline hydrolysis of the corresponding methyl ester (XII) of the trans-ketoacid (XI) with ethylene glycol in the presence of p-toluenesulfonic acid.



When the ethyleneketal of the ketoacid (XIII) was cyclized under the action of hydrogen fluoride, instead of the corresponding tricyclic ketone (III), a substance was formed in quantitative yield, which was insoluble in soda solution and decomposed on distillation. However, this substance dissolved readily in solutions of alkalis; when the solutions obtained were acidified, the trans-ketoacid (XVI) was liberated. Elementary analysis of the substance indicated that it had the same elementary composition ($C_{16}H_{20}O_5$) as the original ethyleneketal of the ketoacid (XIII).

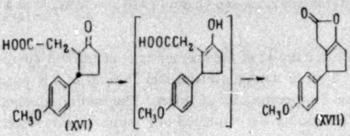
Its infrared spectrum had absorption bands characteristic of hydroxy groups [6] ($3440\ cm^{-1}$) and lactone carbonyl groups [7] ($1738\ cm^{-1}$) (Fig. 1).

The properties of the compound listed indicate that it has the structural formula (XIV). 5-(p-Methoxyphenyl)-8-(β-hydroxy)-ethoxy-2-keto-1-oxa-bicyclo-(0,3,3)-octane (XIV) was characterized as the acetate (XV) prepared by reacting (XIV) with ketone in the presence of sulfoacetic acid as a catalyst. The formation of (XIV) may be represented in the following way:



A case of the isolation of an ethyleneketal in the form of a cyclic ethyleneketal and in the form of the β-hydroxyethyl ether of the enol is described in the literature [8, 9].

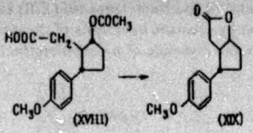
Cyclization of the trans-ketoacid (XVI) both under the action of hydrogen fluoride and by the Friedel-Crafts method also did not lead to the tricyclic diketone (IV), but gave the enol lactone (XVII) by the following scheme:



The formation of the enol lactone was confirmed by the characteristic infrared absorption band for a lactone carbonyl group ($1735\ cm^{-1}$) (Fig. 2). The lactone (XVII) was stable to soda and alkali solution at room temperature. However, with prolonged heating in an alcohol solution of sodium hydroxide, the enol lactone dissolved. When the alkaline solution was acidified, the original trans-ketoacid (XVI) was liberated.

Attempts to prepare the tricyclic ketone (V) by intramolecular acylation of anti-trans-3-(p-methoxyphenyl)-cyclopentane-1-acetoxy-2-acetic acid (XVIII) also did not give positive results. The cyclization was performed by three methods: by the Friedel-Crafts method and under the action of hydrogen fluoride and of polyphosphoric acid. The sole reaction product, which was isolated in quantitative yield, was the lactone of the anti-cis-hydroxyacid (XIX), whose formation from the acetate of anti-trans-hydroxyacid (XVIII) may occur as the result of a

Walden inversion at the carbon atom, connected to the hydroxyl group.



The tendency towards the formation of a lactone ring in the case of a cyclization of the trans-ketoacid (XVI), the ethyleneketal of this acid (XIII) and the acetate of the anti-trans-hydroxyacid (XVIII) indicates that energy considerations favor the formation of a structure with two conjugated five-membered rings, which results in the absence of strain in this system [10].

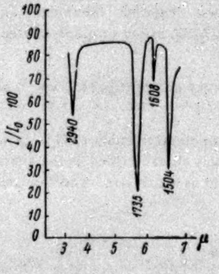


Fig. 1.

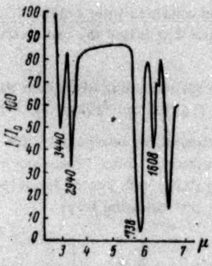


Fig. 2.

## EXPERIMENTAL

Trans-3-(p-methoxyphenyl -cyclopentane-1-ethylenedioxy-2-acetic acid (XIII). A solution of 5 g (0.019 mole) of the methyl ester of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid (XI) and 75 mg of p-toluenesulfonic acid in 50 ml of anhydrous benzene and 2 g (0.032 mole) of ethylene glycol was boiled for 5 hours in a round-bottomed flask, fitted with a Dean and Stark still-head and a reflux condenser with protection against moisture. After cooling, the benzene solution was washed with sodium bicarbonate solution and then saturated sodium chloride solution. Evaporation of the benzene yielded 5.88 g of the methyl ester of trans-3-(p-methoxyphenyl)-cyclopentane-1-ethylenedioxy-2-acetic acid (XII) in the form of a colorless oil, which was hydrolyzed without further purification.

A solution of 5.88 g (0.019 mole) of the methyl ester of trans-3-(p-methoxyphenyl)-cyclopentane-1-ethylenedioxy-2-acetic acid in 55 ml of methyl alcohol and 10.5 ml of 2 N potassium hydroxide solution (0.021 mole) was allowed to stand at room temperature for 15 hours. The methyl alcohol was distilled off in a stream of nitrogen at reduced pressure. The residue was dissolved in a saturated salt solution and acidified with dilute acetic acid until just acid to litmus. The acid liberated was extracted with benzene. The benzene extract was washed with a saturated salt solution and dried over anhydrous sodium sulfate. The residue after evaporation of the solvent (5.6 g) was recrystallized twice from benzene. We obtained 3.6 g (65%) of trans-3-(p-methoxyphenyl)-cyclopentane-1-ethylenedioxy-2-acetic acid (XIII) with m.p. 123-124° in the form of small needles.

Found %: C 65.89; H 6.93. $C_{16}H_{20}O_5$. Calculated %: C 65.73; H 6.89.

Cyclization of trans-3-(p-methoxyphenyl)-cyclopentane-1-ethylenedioxy-2-acetic acid (XIII). 3.5 g of trans-3-(p-methoxyphenyl)-cyclopentane-1-ethylenedioxy-2-acetic acid was treated with 35 g of liquid hydrogen fluoride in a ftorplast* vessel. The reaction mixture was left to stand for 2 hours, then the hydrogen fluoride was removed in a stream of air and the residue dissolved in chloroform. The chloroform extract was washed with water, a 5% solution of sodium carbonate and again with water and dried with sodium sulfate. Evaporation of the chloroform yielded 3.3 g of 5-(p-methoxy)-8-(β-hydroxy)-ethoxy-2-keto-1-oxa-bicyclo-(0,3,3)-octane (XIV) as an immobile oil with a slightly greenish color. The substance decomposed on distillation, even in high vacuum. The substance dissolved quite readily in solutions of alkalis but not in soda solution, indicating the lactone character of the carboxyl group link. Acidification of the alkaline solution precipitated 3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid with m.p. 145.5-146.5° (not depressed with it).

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*See footnote, page 2216.

Found %: C 66.09; H 6.86; OH 5.17. $C_{16}H_{20}O_5$. Calculated %: C 65.73; H 6.89; OH 5.81.

The infrared spectrum indicated the presence of a hydroxyl group (3440 $cm^{-1}$) and a lactone carboxyl group (1738 $cm^{-1}$).

5-(p-Methoxyphenyl)-8-(β-acetoxy)-ethoxy-2-keto-1-oxa-bicyclo-(0,3,3)-octane (XV). Over a period of 2 minutes, a 5-fold amount of ketene was passed into a solution of 0.65 g (0.0022 mole) of 5-(p-methoxyphenyl)-8-(β-hydroxy)-ethoxy-2-keto-1-oxa-bicyclo-(0,3,3)-octane (XIV) and 1 mg of sulfoacetic acid, as catalyst, in 3 ml of anhydrous acetone. The reaction mixture became warm (without the catalyst the reaction did not occur). The excess ketene was expelled with nitrogen. The sulfoacetic acid was neutralized with anhydrous sodium bicarbonate. The residue after evaporation of the acetone was dissolved in absolute ether. The ether solution was filtered and evaporated. We obtained 0.72 g of 5-(p-methoxyphenyl)-8-(β-acetoxy)-ethoxy-2-keto-1-oxa-bicyclo-(0,3,3)-octane (XV) as a colorless oil.

Found %: C 64.62; H 6.65. $C_{18}H_{22}O_6$. Calculated %: C 64.65; H 6.63.

Cyclization of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid (XVI). 3.5 g of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid was treated with 35 g of liquid hydrogen fluoride under the conditions of the experiment described above. After removal of the hydrogen fluoride, the residue was dissolved in chloroform. The chloroform extract was washed with water, 5% sodium hydroxide solution and again with water. After evaporating the chloroform, we obtained 1 g of a substance in the form of an immobile, colorless oil with b.p. 148-150° (0.35 mm). Elementary analysis of the substance and also its capacity for giving trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid on alkaline hydrolysis and the infrared (C = O, 1735 $cm^{-1}$) and ultraviolet spectra ($\lambda_{max}$ $C_2H_5OH$ – 275 mμ, log ε 3.025) indicate that the reaction gave the unsaturated lactone (XVII).

Found %: C 72.87; H 6.21. $C_{14}H_{14}O_3$. Calculated %: C 73.02; H 6.13.

Alkaline hydrolysis regenerated the original ketoacid: 0.2 g of the unsaturated lactone was boiled with 6 ml of 10% potassium hydroxide in methanol for 14 hours.

The residue from evaporation of the methanol in vacuum was dissolved in ether. The original acid was extracted from the ether solution with 5% soda solution and acidification of this liberated a crystalline acid with m.p. 106-107° (not depressed by the original). The ether solution contained nothing.

Cyclization of trans-3-(p-methoxyphenyl)-cyclopentane-1-acetoxy-2-acetic acid (XVIII) was carried out by several methods. a) Friedel - Crafts method: 2.5 g (0.012 mole) of finely powdered phosphorus pentachloride was added to a solution of 0.5 g (0.0017 mole) of trans-3-(p-methoxyphenyl)-cyclopentane-1-acetoxy-2-acetic acid in 10 ml of anhydrous benzene and the mixture stirred at room temperature for 0.5 hours. The reaction mixture was cooled with ice-water and a solution of 3 ml (0.013 mole) of stannic chloride in 6 ml of anhydrous benzene added to it. After being stirred for an hour, the reaction mixture was decomposed with ice-water and dilute hydrochloric acid. The precipitate was extracted with chloroform. The chloroform extract was washed with water, 5% soda solution and again with water and dried. Removal of the solvent gave a quantitative yield of a substance, which, after recrystallization from alcohol, had m.p. 141-142° and did not depress the melting point of the lactone of anti-trans-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid (XIX).

b) Under the action of polyphosphoric acid: to the polyphosphoric acid, prepared from 5 g of phosphorus pentoxide and 3.2 ml of phosphoric acid and heated to 50°, was added 0.5 g of trans-3-(p-methoxyphenyl)-cyclopentane-1-acetoxy-2-acetic acid and the mixture stirred for 15 minutes. The reaction mixture was poured onto ice. Working up in the usual way gave a quantitative yield of the lactone of anti-trans-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid with m.p. 141-142°.

## SUMMARY

A study was made of the cylization of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid, the ethyleneketal of this acid and anti-trans-3-(p-methoxyphenyl)-cyclopentane-1-acetoxy-2-acetic acid using hydrogen fluoride and polyphosphoric acid and by the Friedel-Crafts method.

It was established that in all three cases, cyclization of compounds containing an oxygen function in position 1 proceeds with the formation of the corresponding lactones and not the expected tricyclic ketones.

## LITERATURE CITED

[1] V. I. Maksimov, G. S. Grinenko, J. Gen. Chem. 28, 2179 (1957).*

[2] A. J. Birch, R. Jaeger and R. Robinson, J. Chem. Soc. 1945, 582.

[3] W. Hückel, M. Sachs, G. Vantschulewitsch and F. Nerdel, Lieb. Ann. 518, 155 (1935).

[4] H. Weidlich, Ber.. 81, 41 (1958).

[5] T. Wieland, J. Anner and K. Miescher, Helv. Chim. Acta 36, 376 (1953).

[6] J. Williams, J. Am. Chem. Soc. 75, 4832 (1953).

[7] R. Rasmmussen and R. Brattain, J. Am. Chem. Soc. 71, 1073 (1949).

[8] G. Rosenkranz, S. Kaufmann, and J. Romo, J. Am. Chem. Soc. 71, 3689 (1949).

[9] D. N. Kao, P. Kurafh, J. Am. Chem. Soc 78, 5660 (1956).

[10] J. W. Barret, R. P. Linstead, J. Chem. Soc. 1935, 436.

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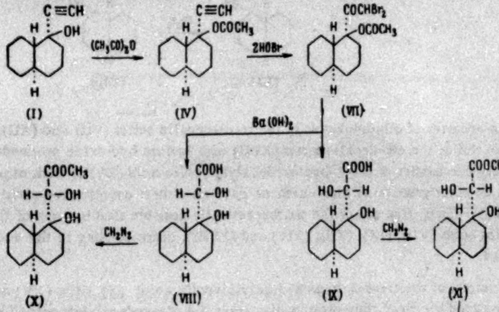
# THE SIMPLEST ANALOGS OF CORTICOSTEROIDS

## III. THE INTRODUCTION OF DIHYDROXYACETONE, GLYCEROL AND DIHYDROXYPROPANECARBOXYLIC ACID SIDE CHAINS INTO DERIVATIVES OF CIS- AND TRANS-DECALINS

I. N. Nazarov,* G. V. Aleksandrova and A. A. Akhrem

In a previous communication [1], the preparation of trans-1-ethynyl-1-decalols (I) and (II), the cis-1-ethynyldecalol (III) and their acetates (IV) – (VI) was described. The present work is devoted to the study of conversion of cis- and trans-1-ethynyldecalols and their acetates into compounds with hydroxyacetone, glycerol and dihydroxypropanecarboxylic acid side chains, using the dibromoketol and glycidol methods, which we developed previously [2], and to the investigation of the stereochemistry of the substances obtained.

The acetate of trans-1-ethynyl-1-decalol (IV) readily added two molecules of hypobromous acid, giving a 92% yield of the acetate of trans-1-dibromoacetyl-1-decalol (VII) [3], which underwent an intramolecular rearrangement of the Favorskii type [2, 4] when saponified with barium hydroxide solution, to form a mixture of isomeric trans-1-hydroxydecalylglycolic acids; fractional crystallization from a mixture of n-heptane and acetone separated the two acids, (VIII) with m.p. 190-191° and (IX) with m.p. 164-165° in a ratio of 1 : 2.



Treatment of the glyceric acids (VIII) and (IX) with an ether solution of diazomethane gave quantitative yields of their methyl esters, (X) with m.p. 124-124.5° and (XI) with m.p. 88-89°.

The addition of hypobromous acid to the acetate of trans-1-ethynyl-1-decalol (V) gave an 85% yield of the acetate of trans-1-dibromoacetyl-1-decalol (XII) as a viscous yellow oil, which decomposed on distillation in vacuum (1 mm); Therefore, the acetate of the dibromoketol (XII) was treated with an aqueous solution of barium hydroxide without isolation in a pure form and this gave a 50% yield of a mixture of two isomeric trans-1-hydroxydecalylglycolic acids, which were fractionally crystallized from a mixture of n-heptane and acetone to separate the individual acids (XIII) with m.p. 138-139° and (XIV) with m.p. 175-175.5° in the ratio 1 : 1.

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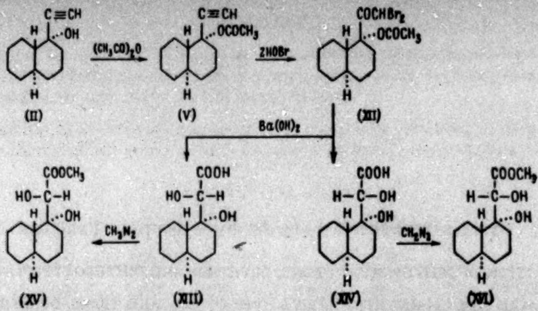
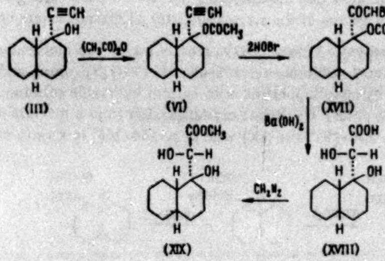


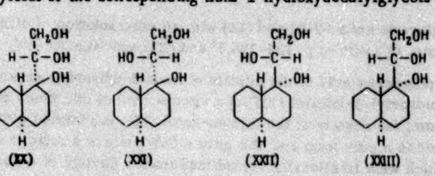
Treatment of the dihydroxyacids (XIII) and (XIV) with an ether solution of diazomethane gave their methyl esters, (XV) with m.p. 123-124° and (XVI) with m.p. 108-109°. As the data presented show, the rearrangement of the acetates of the dibromoketols of the trans-decalin series (VII and XII) during saponification is not stereospecific and proceeds in both possible directions.

Treatment of the acetate of cis-1-ethynyl-1-decalol (VI) with hypobromous acid yielded the acetate of cis-1-dibromoacetyl-1-decalol (XVII).

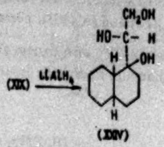


In contrast to the acetates of dibromoketols of the trans-decalin series (VII) and (XII), saponification of the acetate of the dibromoketol of the cis-decalin series (XVII) with barium hydroxide proceeded stereoselectively and gave a 50% yield of only one isomer of cis-1-hydroxydecalylglycolic acid (XVIII) with m.p. 155-156°. Treatment of this acid with an ether solution of diazomethane gave an almost quantitative yield of the methyl ester (XIX) with m.p. 100-101°. Thus, five out of the six theoretically possible steroisomers of the cis- and trans-1-hydroxydecalylglycolic acids (VII), (IX), (XII), (XIV) and (XVIII), corresponding to the acetylenyl alcohols (I) — (III), were synthesized.

Reduction of the esters of the trans-1-hydroxydecalylglycolic acids (X), (XI), (XV) and (XVI) with lithium aluminum hydride gave good yields of the corresponding trans-1-hydroxydecalylglycols (XX) – (XXIII).

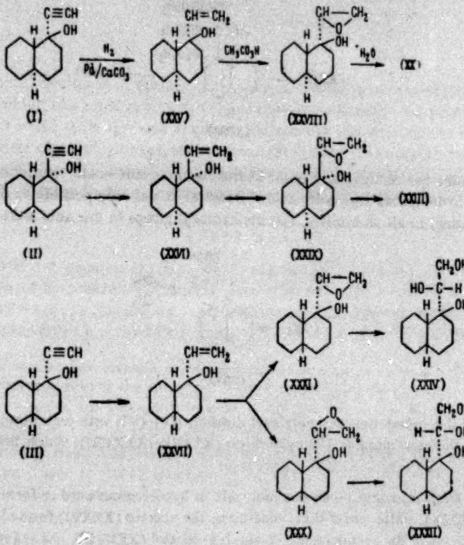


Cis-1-hydroxydecalylglycol (XXIV) was isolated by reduction of the methyl ester of cis-1-hydroxydecalylglycolic acid (XIX).


CH₂OH
HO–C–H
H
OH
(XIX)
LiAlH₄
H
(XXIV)

The second method of introducing a glycerol side chain, which we used in this work, was the glycidol method [2], based on the oxidation of vinyldecalols with peracetic acid to give the corresponding oxides with subsequent hydrolysis of these into derivatives with a glycerol side chain.

The starting 1-vinyl-1-decalols (XXV) – (XXVII) were prepared by catalytic hydrogenation of 1-ethynyl-1-decalols (I) – (III) using palladium on calcium carbonate at atmospheric pressure [5].


C≡CH
H
OH
H
(I)
H₂
Pd/CaCO₃
CH=CH₂
H
OH
H
(XXV)
CH₃CO₃H
CH–CH₂
O
H
OH
H₂O
H
(XXVIII)
(XX)
C≡CH
H
OH
H
(II)
CH=CH₂
H
OH
H
(XXVI)
CH–CH₂
O
H
OH
H
(XXIX)
(XXIII)
CH–CH₂
O
H
OH
H
(XXXI)
CH₂OH
HO–C–H
H
OH
H
(XXIV)
C≡CH
H
OH
H
(III)
CH=CH₂
H
OH
H
(XXVII)
O
CH–CH₂
H
OH
H
(XXX)
CH₂OH
H–C–OH
H
OH
H
(XXXII)

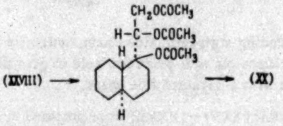
By oxidation of trans-1-vinyl-1-decalols (XXV) and (XXVI) with peracetic acid in chloroform we obtained good yields of trans-1-hydroxydecalylethylene oxides (XXVIII) with m.p. 116-117° and (XXIX) with m.p. 112-114°. Hydrolysis of the latter compounds with dilute acetic acid formed the triols (XX) and (XXIII), which were described above and obtained by reduction of the methyl esters of trans-1-hydroxydecalylglycolic acids (X) and (XVI).

Oxidation of cis-1-vinyl-1-decalol (XXVII) with peracetic acid produced a mixture of isomeric cis-1-hydroxydecalyl-1-ethylene oxides, from which we isolated the individual cis-glycidols (XXX) with m.p. 90-91° and (XXXI) with m.p. 100-101° in a ratio of 1 : 1 by fractional crystallization from isooctane.

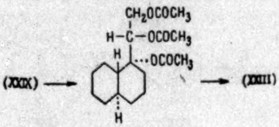
Thus, oxidation of the vinyl alcohols of the trans-decalin series (XXV) and (XXVI) proceeded stereospecifically and led, in each case, to the formation of only one glycidol, while oxidation of the vinyl alcohol of the cis-decalin series (XXVII) was not stereospecific and gave both possible stereoisomers of the glycidol in equal amounts.

When treated with dilute acetic acid, the cis-glycidols (XXX) and (XXXI) formed the cis-triols (XXXII) with m.p. 115-117° and (XXIV) with m.p. 109-111°. As mentioned above, the latter was also obtained by reducing the methyl ester of cis-1-hydroxydecalylglycolic acid (XIX) with lithium aluminum hydride. Thus, using the dibromoketol and the glycidol methods, we were able to synthesize all six theoretically possible stereoisomers of the cis- and trans-1-hydroxydecalylglycols (XX) - (XXIV) and (XXXII), corresponding to the 1-ethynyl-1-decalols (I) - (III).

Boiling the trans-glycidols (XXVIII) and (XXIX) with excess acetic anhydride formed the triacetates (XXXIII) and (XXXIV), which were hydrolyzed with potassium hydroxide in aqueous methanol to form the triols (XX) and (XXIII) described above.

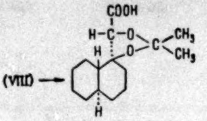


(XXXIII)



(XXXIV)

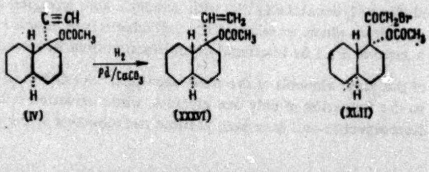
In order to determine the configuration of the hydroxyls in the side chain, attempts were made to prepare acetonates [7] of the 1-hydroxydecalylglycolic acids. However, it was only possible to obtain an acetonate (XXXV) from acid (VIII), indicating, in all probability, that the hydroxyl groups in this acid were sterically adjacent.



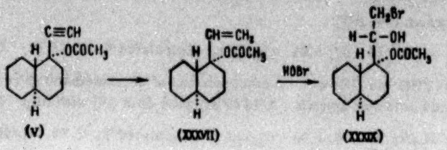
(XXXV)

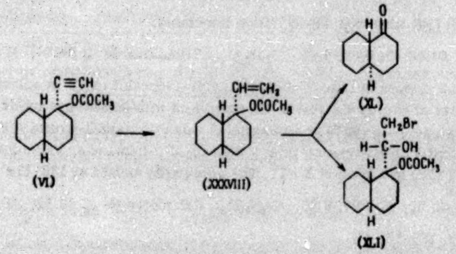
Hydrogenation of the acetates of the acetylenyl alcohols (IV)-(VI) with palladium on calcium carbonate yielded the acetates of the corresponding 1-vinyldecalols (XXXVI)-(XXXVIII), which behaved differently towards hypobromous acid.

The acetate (XXXVII) smoothly added one molecule of hypobromous acid to form the crystalline acetate of the bromohydrin (XXXIX), while, under these conditions, the acetate (XXXVI) formed an oil, which decomposed on vacuum distillation. When the acetate of cis-1-vinyl-1-decalol (XXXVIII) was reacted with hypobromous acid, the main product isolated was trans-α-decalone (XL) and only minute amounts of a crystalline substance were formed and this was close in analysis to the acetate of the bromohydrin (XLI). Many attempts to oxidize the bromohydrin (XXXIX) into the corresponding α-bromoketol (XLII) and to substitute the bromine in it by a hydroxyl or an acetoxyl group were unusccessful: in all cases, the bromohydrin (XXXIX) was recovered from the reaction unchanged.



(IV) (XXXVI) (XLII)





Thus, the great steric hindrance of the side chain in trans-1-ethynyl-1-decalol (II) in comparison with the acetylenyl alcohol (I), which was noted previously [1] and appears for example in hydration reactions, was further confirmed in the present work. This appeared as greater hindrance to saponification of the acetate of the dibromoketol (XII), in the inability of the dihydroxyacids (XIII) and (XIV) to form acetonates, worse results in the oxidation of the vinyl alcohol (XXVI) into the glycidol (XXIX) and, finally, in the impossibility of oxidizing the hydroxyl group in bromohydrin (XXXIX) and substituting the bromine atom in it by a hydroxyl or an acetoxyl group.

## EXPERIMENTAL

The starting 1-ethynyl-1-decalols (X) (b.p. 86-87° at 1 mm, $n^{22.5}D$ 1.5033), (II) (m.p. 54-55°) and (III) (m.p. 55-56°) were prepared by condensation of trans- and cis-α-decalones with sodium acetylide in liquid ammonia solution, as described in [1]. Boiling the acetylenyl alcohols (I)-(III) with excess acetic anhydride [6] yielded the corresponding acetates: (IV) (m.p. 79-80°), (V) (b.p. 106-108° at 2 mm, $n^{20.5}D$ 1.4940) and (VI) (m.p. 65-67°) [1].

Addition of hypobromous acid to the acetate of trans-1-ethynyl-1-decalol (IV). 2 ml of a glacial, acetic acid and 1.5 g of sodium acetate was added to a mixture of 2.3 g of acetamide, 6 ml of water, 2.5 g of chalk and 3.6 g of bromine. A solution of 1.4 g of acetate (IV) (m.p. 79-80°) in 17 ml of trimethylcarbinol was added rapidly with stirring to the solution of N-bromoacetamide obtained. The mixture warmed up slightly. The reaction mixture was cooled to 20° and stirred at this temperature for 2.5 hours. The crystalline precipitate was separated and recrystallized from isooctane. We obtained 2.3 g (92%) of the acetate of trans-1-dibromoacetyl-1-decalol (VII) with m.p. 92-93° [2].

Addition of hypobromous acid to the acetate of trans-1-ethynyl-1-decalol (V). By the method described above, from 5 g of acetate (b.p. 104-106° at 2 mm, $n^{20.5}D$ 1.4940), we obtained 7.6 g (85%) of the acetate of trans-1-dibromoacetyl-1-decalol (XII) as an oil with $n^{20}D$ 1.5278, which decomposed on distillation in vacuum and was used for saponification without further purification (see below).

Saponification of the acetate of trans-1-dibromoacetyl-1-decalol (VII). A solution of 2 g of dibromoketol (VII) (m.p. 92-93°) in 10 ml of trimethylcarbinol was poured into a hot solution of 1.3 g of barium hydroxide in 10 ml of water and the mixture boiled for 5 hours. When the mixture had been cooled, the precipitate was filtered off and recrystallized from isooctane to yield 0.4 g of the starting acetate of the dibromoketol (m.p. 92-93°); the aqueous layer was acidified with dilute hydrochloric acid, carefully extracted with ether and the ether solution dried with magnesium sulfate. After removing the solvent we obtained 0.45 g (50%) of crystals with m.p. 157-160°, which were a mixture of the isomeric trans-1-hydroxydecalylglycolic acids and separation of these by fractional crystallization from a mixture of n-heptane and acetone gave the two individual stereoisomeric acids (VIII) and (IX) in the ratio 1 : 2. The acid (VIII) melted at 190-191°.

Found %: C 62.90, 63.16; H 8.82, 8.81. $C_{12}H_{20}O_4$. Calculated %: C 63.12; H 8.84.

The acid (IX) melted at 164-165°.

Found %: C 62.98; 63.16; H 8.97, 8.94. $C_{12}H_{20}O_4$. Calculated %: C 63.12; H 8.84.

Treatment of acids (VIII) and (IX) with an ether solution of diazomethane gave a quantitative yield of their methyl esters, which formed colorless crystals. Acid (VIII) gave ester (X) with m.p. 124-124.5° (from isooctane).

Found %: C 64.28, 64.23; H 9.04, 9.04. $C_{13}H_{22}O_4$. Calculated %: C 64.44; H 9.15.

Acid (IX) gave ester (XI) with m.p. 88-89° (from isooctane).

Found %: C 64.11, 64.00; H 9.02, 9.11. $C_{13}H_{22}O_4$. Calculated %: C 64.44; H 9.15.

Saponification of the acetate of trans-1-dibromoacetyl-1-decalol (XII). A solution of 2 g of dibromoketol (XII) ($n^{20}D$ 1.5278) in 10 ml of trimethylcarbinol was saponified with barium hydroxide as described in the previous experiment. We thus obtained 0.5 g (55%) of a mixture of isomeric trans-1-hydroxydecalylglycolic acids and separation of this by fractional crystallization from a mixture of n-heptane and acetone gave two individual stereoisomeric acids (XIII) and (XIV) in a ratio of 1 : 1. The acid (XIII) melted at 138-139°.

Found %: C 63.49, 63.20; H 8.99, 8.86. $C_{12}H_{20}O_4$. Calculated %: C 63.12; H 8.84.

Acid (XIV) had m.p. 175-175.5°.

Found %: C 63.20, 63.40; H 8.79, 8.89. $C_{12}H_{20}O_4$. Calculated %: C 63.12; H 8.84.

When treated with an ether solution of diazomethane, the hydroxydecalylglycolic acids isolated readily formed their methyl esters. Acid (XIII) gave colorless crystals of ester (XV) with m.p. 123-124° (from isooctane).

Found %: C 64.37, 64.34; H 9.09, 9.22. $C_{13}H_{22}O_4$. Calculated %: C 64.44; H 9.15.

Acid (XIV) gave ester (XVI) as colorless crystals with m.p. 108-109° (from isooctane).

Found %: C 64.44, 64.24; H 9.24, 9.17. $C_{13}H_{22}O_4$. Calculated %: C 64.44; H 9.15.

A mixture of esters (X) and (XV) melted at 100-102°.

Addition of hypobromous acid to the acetate of cis-1-ethynyl-1-decalol (VI). The addition of hypobromous acid to 2 g of acetate (VI) (m.p. 65-67°) by the method described above, yielded 3 g (85.7%) of the acetate of cis-1-dibromoacetyl-1-decalol (XVII), as coarse, clear crystals with m.p. 90-91° (from isooctane).

Found %: C 42.55, 42.43; H 5.07, 5.04; Br 40.56, 40.58. $C_{14}H_{20}O_3Br_2$. Calculated %: C 42.44; H 5.01; Br 40.35.

Saponification of the acetate of cis-1-dibromoacetyl-1-decalol (XVII). A solution of 2 g of the dibromoketol (XVII) (m.p. 90-91°) in 20 ml of trimethylcarbinol and 20 ml of dioxane was poured into a hot solution of 3 g of barium hydroxide in 25 ml of water. The mixture was boiled for 4 hours at 86°, acidified with 5 ml of dilute hydrochloric acid and carefully extracted with ether and the ether solution dried with magnesium sulfate. We obtained 0.6 g (50%) of cis-1-hydroxydecalylglycolic acid (XVIII) as colorless crystals with m.p. 155-156° (from a mixture of isooctane and dioxane).

Found %: C 63.25, 63.37; H 8.80, 8.89. $C_{12}H_{20}O_4$. Calculated %: C 63.12; H 8.84.

The methyl ester (XIX), obtained by treating acid (XVIII) with an ether solution of diazomethane, formed colorless crystals with m.p. 100-101° (from isooctane).

Found %: C 64.44, 64.24; H 9.24, 9.17. $C_{13}H_{22}O_4$. Calculated %: C 64.44; H 9.15.

Reduction of trans-1-hydroxydecalylglycolic esters with lithium aluminum hydride. a) A solution of 100 mg of ester (X) (m.p. 124-124.5°) in 20 ml of ether was added to a solution of 1.5 g of $LiAlH_4$ in 100 ml of absolute ether at such a rate that the mixture boiled evenly. The mixture was then stirred for 10 hours at 20° and 10 hours at the boiling point of ether. The excess lithium aluminum hydride was destroyed at 20° with 5 ml of ethyl acetate and then 25 ml of 5% sulfuric acid. The ether layer was separated, the aqueous layer carefully extracted with ether and the ether extracts dried with magnesium sulfate. After removing the solvent, we obtained 65 mg (68.4%)

of trans-1-hydroxydecalylglycol (XX) as colorless crystals with m.p. 117-118° (from a mixture of ethyl acetate and isooctane).

Found %: C 67.54, 67.40; H 10.32, 10.40. $C_{12}H_{22}O_3$. Calculated %: C 67.20; H 10.34.

b) Under the same conditions, 200 mg of ester (XI) (m.p. 88-89°) yielded 150 mg (79%) of trans-1-hydroxydecalylglycol (XXI) as colorless crystals with m.p. 119-120° (from a mixture of ethyl acetate and isooctane).

Found %: C 67.39, 67.54; H 10.46, 10.38. $C_{12}H_{22}O_3$. Calculated %: C 67.20; H 10.34.

A mixture of these triols melted at 99-103°.

c) Reduction of 100 mg of ester (XV) (m.p. 123-124°) with $LiAlH_4$ produced 60 mg (63%) of trans-1-hydroxydecalylglycol (XXII) as colorless crystals with m.p. 92-93° (from a mixture of isooctane and ethyl acetate).

Found %: C 67.30; 67.51; H 10.30, 10.31. $C_{12}H_{22}O_3$. Calculated %: C 67.20; H 10.34.

d) Reduction of 250 mg of ester (XVI) (m.p. 108-109°) with lithium aluminum hydride yielded 200 mg (84.3%) of trans-1-hydroxydecalylglycol (XXIII) as colorless crystals with m.p. 158-159° (from a mixture of ethyl acetate and isooctane).

Found %: C 67.55, 67.39; H 10.33, 10.44. $C_{12}H_{22}O_3$. Calculated %: C 67.20; H 10.34.

Reduction of the ester of cis-1-hydroxydecalylglycolic acid (XIX) with lithium aluminum hydride. When 200 mg of the ester (XIX) (m.p. 100-101°) was reduced with a four-fold excess of lithium aluminum hydride we obtained 120 mg of cis-1-hydroxydecalylglycol (XXIV) as colorless crystals with m.p. 109-111° (from isooctane).

Found %: C 67.46, 67.53; H 10.21, 10.34; $C_{12}H_{22}O_3$. Calculated %: C 67.20; H 10.34.

Hydrogenation of trans-1-ethynyl-1-decalols. a) A solution of 7.5 g of the acetylenyl alcohol (I) (b.p. 86-87° at 1 mm, $n^{22.5}D$ 1.5033) in 50 ml of ethanol was hydrogenated over palladium on calcium carbonate until 1100 ml of hydrogen (at 748 mm and 28°) had been absorbed. We obtained 6.5 g (86.6%) of trans-1-vinyl-1-decalol (XXV) as a colorless liquid.

B.p. 73.5° (1 mm), $n^{19.5}D$ 1.5010; $\nu$ 996, 1005, 1015, 1027, 1143 and 1162 $cm^{-1}$.

b) Under the same conditions, from 6 g of the acetylenyl alcohol (II) (m.p. 54-55°) we obtained 5.1 g (85%) of trans-1-vinyl-1-decalol (XXVI) as a colorless liquid.

B. p. 80° (1 mm), $n^{23}D$ 1.5050, $d^{20}_4$ 0.9952, $MR_D$ 53.84; calc. 54.27.

$\nu$ 992, 1012, 1089, 1102, 1141 and 1160 $cm^{-1}$.

Found %: C 80.17, 79.96; H 11.26, 11.32. $C_{12}H_{20}O$. Calculated %: C 79.93; H 11.18.

Hydrogenation of cis-1-ethynyl-1-decalol (III). A solution of 7.5 g of cis-acetylenyl alcohol (III) (m.p. 55-56°) in 30 ml of ethanol was hydrogenated over palladium on calcium carbonate until 1100 ml of hydrogen (at 718 mm, 23°) had been absorbed. We obtained 6.75 g (90%) of cis-1-vinyl-1-decalol (XXVII) as a colorless liquid.

B. p. 85-87° (1 mm). $n^{20}D$ 1.5098, $d^{20}_4$ 1.0019, $MR_D$ 54.00; calc. 54.27.

Found %: C 79.94, 80.02; H 11.44, 11.40. $C_{12}H_{20}O$. Calculated %: C 79.93; H 11.18.

Oxidation of trans-1-vinyl-1-decalols with peracetic acid. a) To a solution of 4.5 g of the vinyl alcohol (XXV) (b.p. 73.5° at 1 mm, $n^{19.5}D$ 1.5010) in 50 ml of chloroform was added 4.5 g of 98% peracetic acid and the mixture kept for 48 hours at 20°. The chloroform layer was then separated, washed twice with sodium bicarbonate solution and dried with magnesium sulfate. After removing the solvent, we obtained 4.3 g (93%) of the trans-glycidol (XXVIII), which crystallized as lustrous, colorless, fine platelets with m.p. 116-117° (from isooctane).

Found %: C 73.35, 73.43; H 10.27, 10.29. $C_{12}H_{20}O_2$. Calculated %: C 73.42; H 10.27.

b) Under the same conditions 4.5 g of the vinyl alcohol (XXIV) (b.p. 80° at 1 mm, $n^{23}D$ 1.5050) yielded 4.5 g of an oil, from which we isolated 3.1 g (75%)* of the trans-glycidol (XXIX), which formed coarse, transparent crystals with m.p. 112-114° (from isooctane).

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* The yield given is calculated on the vinyldecalol, which reacted.

Found %: C 73.48, 73.41; H 10.24, 10.16. $C_{12}H_{20}O_2$. Calculated %: C 73.42; H 10.27.

Chromatography of 1 g of the mother liquor on aluminum oxide yielded 0.7 g of the starting vinyldecalol ( (XXVI), $n^{21}D$ 1.5056.

A mixture of these two trans-glycidols melted at 85-87°.*

Oxidation of cis-1-vinyl-1-decalol (XXVII) with peracetic acid. To a solution of 6 g of the vinyl alcohol (XXVII) (b.p. 85-87° at 1 mm, $n^{20}D$ 1.5098) in 50 ml of chloroform was added 7 ml of 90% peracetic acid and the mixture kept at 20° for 48 hours. The mixture was then washed with water and twice with sodium bicarbonate solution and the chloroform solution dried with magnesium sulfate. After removing the solvent, we obtained 3 g (50%) of a mixture of isomeric cis-glycidols with m.p. 63-67° and fractional crystallization of this from isooctane gave two individual stereoisomeric glycidols (XXX) and (XXXI) in the ratio 1 : 1. Glycidol (XXX) crystallized in the form of right tetrahedra with m.p. 90-91°.

Found %: C 73.39, 73.38; H 10.21, 10.18. $C_{12}H_{20}O_2$. Calculated %: C 73.42; H 10.27.

Glycidol (XXXI) crystallized in the form of prisms with m.p. 100-101°.

Found %: C 73.22, 73.30; H 10.15, 10.20. $C_{12}H_{20}O_2$. Calculated %: C 73.42; H 10.27.

A mixture of cis-glycidols (XXX) and (XXXI) melted at 67-68°.

Hydrolysis of trans-glycidols (XXVIII) and (XXIX). a) A solution of 300 mg of glycidol (XXVIII) (m.p. 116-117°) in 10 ml of dioxane was added to a solution of 6 ml of glacial acetic acid in 25 ml of water and the mixture boiled for 4 hours. The cooled mixture was neutralized with soda solution and extracted with ether and the ether extract dried with magnesium sulfate. Removal of the ether and recrystallization of the residue from a mixture of ethyl acetate and isooctane yielded 210 mg (64%) of trans-1-hydroxydecalylglycol (XX) with m.p. 117-118°, undepressed by the sample described above, prepared by reducing ester (X) with $LiAlH_4$.

b) Under the same conditions, 500 mg of glycidol (XXIX) (m.p. 112-114°) yielded 400 mg (75%) of trans-1-hydroxydecalylglycol (XXIII) (m.p. 156-158°), undepressed by the sample prepared by reducing the methyl ester (XVI) with lithium aluminum hydride.

Hydrolysis of cis-1-hydroxydecalylethylene oxides (XXX) and (XXXI). a) A solution of 300 mg of glycidol (XXX) (m.p. 90-91°) in 8 ml of trimethylcarbinol was poured into a hot solution of 25 ml of acetic acid in 25 ml of water and the mixture boiled for 5 hours at 86°. The mixture was neutralized with soda solution and extracted three times with ether and the ether solution dried with magnesium sulfate. We obtained 190 mg (60%) of cis-1-hydroxydecalylglycol (XXXII) as colorless crystals with m.p. 115-117° (from isooctane).

Found %: C 67.38, 67.31; H 10.30, 10.29. $C_{12}H_{22}O_3$. Calculated %: C 67.20; H 10.34.

A mixture with original glycidol (m.p. 90-91°) melted at 73-75°.

b) Under the same conditions, 300 mg of glycidol (XXXI) (m.p. 100-101°) gave 190 mg (60%) of the triol (XIX) with m.p. 109-111°, undepressed by the sample obtained by reducing cis-1-hydroxydecalylglycolic ester (XIX) with $LiAlH_4$. A mixture of triol (XXIV) and the original glycidol (XXXI) melted at 82-85°. Mixtures of triol (XXIV) with cis-glycidol (XXX) and with cis-triol (XXXII) melted at 81-85° and 73-75°, respectively.

Preparation of triacetates of trans-triols (XX) and (XXIII). a) A solution of 1.7 g of trans-glycidol (XXVIII) (m.p. 116-117°) in 10 ml of acetic anhydride was boiled under reflux for 6 hours in the presence of 0.1 g of potassium acetate. After removal of the excess acetic anhydride, the residue was diluted with ether and the potassium acetate filtered off; the ether extract was washed with soda solution and dried with magnesium sulfate. After removal of the ether, the residue was vacuum-distilled. We obtained 1.8 g (62%) of the triacetate of the trans-triol (XXXIII) as a very viscous, colorless oil. The b.p. was 140-144° (1 mm), $n^{23}D$ 1.4782.

Found %: C 63.80, 63.80; H 8.49, 8.39. $C_{18}H_{28}O_6$. Calculated %: C 63.51; H 8.29.

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* Oxidation of the crude mixture of trans-1-vinyl-1-decalols with peracetic acid gave a 90% yield of a mixture of trans-glycidols with m.p. 86-89°, which were fractionally crystallized from isooctane to isolate the same individual glycidols: (XXVIII) (m.p. 116-117°) and (XXIX) (m.p. 112-114°) in the ratio 5 : 4.

When the triacetate obtained (XXXIII) was shaken with potassium hydroxide in aqueous methanol for 4 hours, we obtained a quantitative yield of the trans-triol (XX) (m.p. 119-119.5°), undepressed by the samples obtained by hydrolysis of the glycidol (XXVIII) and reduction of ester of the glyceric acid (X). A mixture with the original trans-glycidol (XXVIII) melted at 93-100°.

b) Under the same conditions, the trans-glycidol (XXIX) (m.p. 112-114°) yielded the triacetate of the trans-triol (XXXIV), which, without isolation in a pure form, was saponified into the trans-triol (XXIII) with m.p. 155-156°, obtained previously.

*Preparation of acetonate of trans-1-hydroxydecalylglycolic acid (VIII).* A solution of 50 mg of the acid (VIII) (m.p. 190-191°) in 7 ml of anhydrous acetone was shaken for 40 hours in the presence of 300 mg of anhydrous copper sulfate. The inorganic precipitate was filtered off, the acetone removed in vacuum and the residue heated on a boiling water bath for 15 minutes at 1 mm. We obtained 30 mg of the acetonate of trans-1-hydroxydecalylglycolic acid (XXXV) as colorless crystals with m.p. 124-125° (from isooctane).

Found %: C 67.33; H 9.15. $C_{15}H_{24}O_4$. Calculated %: C 67.13; H 9.02.

*Hydrogenation of acetates of trans-1-ethynyl-1-decalols.* a) A solution of 4.4 g of acetate (IV) (m.p. 79-80°) in a mixture of 25 ml of alcohol and 5 ml of dioxane was hydrogenated over a palladium catalyst until one mole of hydrogen had been absorbed (739 mm, 18°). We obtained 3.25 g (75%) of the acetate of trans-1-vinyl-1-decalol (XXXVI) as a colorless liquid.

B. p. 100-102° (3 mm), $n^{16.5}D$ 1.4815.

Found %: C 75.82, 75.74; H 10.12, 10.05. $C_{14}H_{22}O_2$. Calculated %: C 75.62; H 9.97.

b) Under the same conditions, 14.2 g of acetate (V) (b.p. 104-106° at 2 mm, $n^{20.5}D$ 1.4940) yielded 11.75 g (83%) of the acetate of trans-1-vinyl-1-decalol (XXXVII) as a colorless liquid.

B. p. 102-104° (3 mm), $n^{16.5}D$ 1.4882, $d^{20}_4$ 1.0042, $MR_D$ 63.63; calc. 63.52.

Found %: C 75.86, 75.87; H 10.37, 10.32. $C_{14}H_{22}O_2$. Calculated %: C 75.62; H 9.97.

*Addition of hypobromous acid to the acetates of trans-1-vinyl-1-decalols.* a) To a solution of N-bromoacetamide, prepared from 10 g of acetamide and 14 g of bromine in 40 ml of water, was added 10 g of sodium acetate and 10 ml of acetic acid, followed by 10 g of acetate (XXXVII) (b.p. 102-104° at 3 mm, $n^{16.5}D$ 1.4882). The mixture was stirred for 1.5 hours, the precipitated product separated from the aqueous layer and dissolved in ether and the solution washed with sodium bicarbonate and dried with magnesium sulfate. After removal of the solvent, we isolated 3.35 g of the acetate of trans-1-(1'-hydroxy-2-bromoethyl)-1-decalol (XXXIX) as colorless needles with m.p. 140-141° (from isooctane).

Found %: C 52.49, 52.49; H 7.29, 7.30; Br 25.43, 25.18. $C_{14}H_{23}O_3Br$. Calculated %: C 52.67; H 7.26; Br 25.31.

b) By treating acetate (XXXVI) (b.p. 100-102° at 3 mm, $n^{16.5}D$ 1.4815) similarly, we obtained a viscous oil with $n^{18.5}D$ 1.530, which decomposed on vacuum-distillation.

*Hydrogenation of the acetate of cis-1-ethynyl-1-decalol (VI).* A solution of 4.8 g of acetate (VI) (m.p. 65-67°) in 25 ml of alcohol was hydrogenated over palladium on calcium carbonate until one mole of hydrogen had been absorbed (749.5 mm, 20°). We obtained 3.8 g (80%) of the acetate of cis-1-vinyl-1-decalol (XXXVIII) as a colorless liquid.

B. p. 97-99° at 1 mm, $n^{20}D$ 1.4862, $d^{20}_4$ 1.0110, $MR_D$ 63.16; calc. 63.52.

Found %: C 75.13, 75.28; H 10.62, 10.66. $C_{14}H_{22}O_2$. Calculated %: C 75.62; H 9.97.

*Reaction of the acetate of cis-1-vinyl-1-decalol (XXXVIII) with hypobromous acid.* When 3.3 g of the acetate (XXXVIII) (b.p. 97-99° at 1 mm, $n^{20}D$ 1.4862) was treated with an aqueous solution of N-bromoacetamide, we isolated 1 g of trans-α-decalone (XL) (m.p. 32-33°) and 0.5 g of a bromine-containing substance with m.p. 137-139°, whose analysis was close to that of the acetate of cis-1-(1'-hydroxy-2-bromoethyl)-1-decalone (XL).

## SUMMARY

A study was made of the dibromoketol and glycidol methods of introducing glycerol and dihydroxycarboxylic acid side chains into the molecules of cis- and trans-α-decalones. Six stereoisomers of trans- and cis-1-hydroxydecalylglycol (erythro – threo-isomerism), four isomeric 1-hydroxydecalylethylene oxides (erythro – threo-isomerism) and five stereoisomeric 1-hydroxydecalyglycolic acids (erythro – threo-isomerism) of the trans-decalin series were isolated.

## LITERATURE CITED

[1] I. N. Nazarov, G. V. Aleksandrova and A. A. Akhrem. J. Gen. Chem. 28, 2199 (1958).*

[2] I. N. Nazarov, A. Akhrem, J. Gen. Chem. 26, 1186 (1956).*

[3] L. E. Coles, W. H. Linnell, et al., J. Chem. Soc. 1954, 2617.

[4] A. E. Favorskii, J. pr. Ch. (2) 88, 658 (1913).

[5] I. N. Nazarov et al, Bull Acad. Sci. USSR, Div. Chem. Sci. 1946, 305.

[6] H. Rupe and W. Messner, et al, Helv. Chim. Acta 11, 449 (1928).

[7] R. B. Woodward, and F. Sondheimer, et al, J. Am. Chem. Soc. 74, 4223 (1952).

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# SYNTHESIS AND TRANSFORMATIONS OF CIS- AND TRANS-1-ETHYNYL-1-DECALOLS

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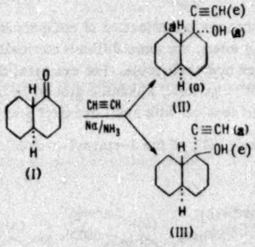
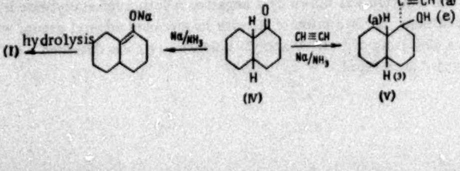
In recent years, chemists of many countries have become interested in the synthesis of simple analogs of steroid hormones and, in particular, of corticosteroids. Papers in this field have been published on derivatives of cyclohexane [1-3], methylcyclohexane [4, 5], cyclopentane [6], perhydroindane and decalin [7, 8], dealing with methods of introducing dihydroxyacetonyl and glyceryl side chains, which are characteristic of natural corticoid hormones. In a number of cases compounds were obtained which showed considerable corticoid activity [5, 9, 10]. In this connection, interest was aroused in a detailed investigation of the condensation of cis- and trans-α-decalones with acetylene, with the object of using the resulting acetylenic alcohols for introducing oxygen-containing side chains into the decalin nucleus, by the method developed in our laboratories [11].

The condensation of trans-α-decalone (I) with acetylene was carried out in the presence of powdered caustic potash under pressure [12] and in solution in liquid ammonia in the presence of sodium [13]. In the latter case, a 90% yield was obtained of a mixture of isomeric trans-1-ethynyl-1-decalols, from which, by freezing out at − 70° and chromatography of the residue on alumina, the epimeric trans-1-ethynyl-1-decalols (II) and (III) were isolated in the ratio of 1 : 2.



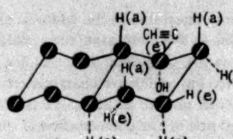
It is well known that cis-α-decalone readily isomerizes under the influence of acid or alkali to trans-α-decalone [14, 15], so it was reasoned that it would be impossible to obtain the cis-1-ethynyl-1-decalols in the strongly alkaline conditions of acetylenic synthesis by A. E. Favorskii's method. But, by carrying out the reaction of cis-α-decalone (IV) with sodium acetylide in solution in liquid ammonia, it was found that the condensation with acetylene successfully competed with the isomerization reaction, and an over-all 60% yield of cis-1-ethynyl-1-decalol (V) was obtained.



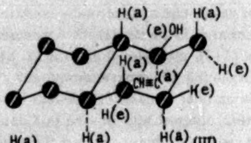
Only about 10% of the cis-α-decalone (IV) was isomerized and recovered in the form of trans-α-decalone (I).

The fact that trans-α-decalone, and not the trans-acetylenic alcohol, was recovered from the reaction mixture conflicts with the enol mechanism for the acetylenic synthesis and again supports the correctness of the metal-organic mechanism for this reaction [12]. The sterically selective course of the acetylenic synthesis in the case of cis-α-decalone, with the formation of only one cis-1-ethynyl-decalol (V), is in agreement with the results of the previously described addition reactions to the carboxyl group of cis-α-decalone [16].

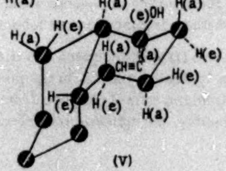
It is now generally accepted that the conformation of cis- and trans-decalins is determined by the conjunction of the two cyclohexane rings in the form of a "chair" [17], in which there are two geometrically non-equivalent forms of bondsbetween carbon atoms and substituents, occupying equatorial (e) or axial (a) positions [18]. Corresponding to this, the conformations of the three isomeric-1-ethyl-1-decalols (II), (III) and (V) obtained by us can be represented by the following models:



(II)



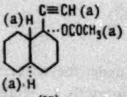
(III)



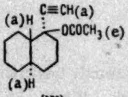
(V)

It is known from the literature that the esterification of compounds with axially disposed hydroxyl groups, and the hydrolysis of the corresponding esters, are more difficult sterically than the corresponding reactions of compounds containing equatorially disposed hydroxyl groups. For example, the acid phthalates, obtained from trans-α- and trans-β-decalols [19, 20], with equatorial alcoholic groups, hydrolyze 19 and 7 times, respectively, more quickly than the esters of the epimeric decalols with axial hydroxyl groups.

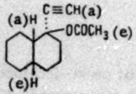
Acetylation, with acetic anhydride [21], of the 1-ethynyl-1-decalols (II), (III) and (V) gave high yields of the corresponding acetates (VI)-(VIII)



(VI)

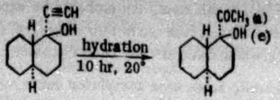


(VII)

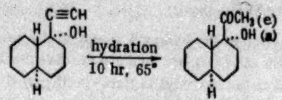


(VIII)

When comparative experiments were carried out on the rates of hydration of the acetylenic alcohols (II), (III) and (V), in aqueous methanol in the presence of mercuric sulfate, it was found that III, with the least-screened ethylidene group, was completely hydrolyzed even at 20° after 10 hours, giving an 80% yield of trans-1-acetyl-1-decalol (IX); the end of the reaction was shown by a negative reaction for acetylenic hydrogen with $AgNO_3$ and $NH_3$. Under the same conditions, the hydration of II, with its screened ethynyl group, was achieved only by boiling at 65° for 10 hours, when a 63% yield of trans-1-acetyl-1-decalol (X) was obtained. At 20°, II was not hydrated and was completely recovered, unchanged.


C≡CH
H
OH
hydration
10 hr, 20°
COCH₃ (a)
OH (e)
H
H

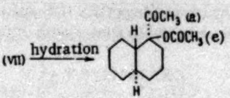
(III) (IX)


C≡CH
H
...OH
hydration
10 hr, 65°
COCH₃ (e)
...OH (a)
H
H

(II) (X)

Similar results were obtained for the hydration of the acetates (VI) and (VII).

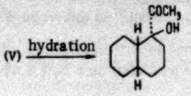
Hydration of VII for 4 hours at 65° gave a 73% yield of the acetate of trans-1-acetyl-1-decalol (XI) [7], while, after the same treatment, VI was recovered unchanged.


(VII)
hydration
COCH₃ (a)
H
OCOCH₃ (e)
H

(XI)

Trans-1-acetyl-1-decalol (IX), with its unscreened axial acetyl group, readily formed both a semicarbazone and a 2,4-dinitrophenylhydrazone, while the fact that trans-1-acetyl-1-decalol (X) only formed a semicarbazone, and that with great difficulty, provided evidence of the screening of the equatorial acetyl group in this compound.

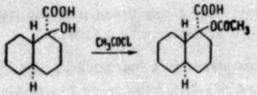
V was also not hydrated at 20°, but an hour's boiling at 65° was sufficient to give a 70% yield of cis-1-acetyl-1-decalol (XII), which only gave a semicarbazone with difficulty and did not form a 2,4-dinitrophenylhydrazone.


(V)
hydration
COCH₃
H
OH
H

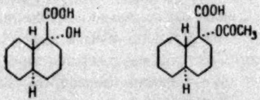
(XII)

These results show that carbon side chains in compounds V and XII are also appreciably screened by the adjacent cyclohexane rings.

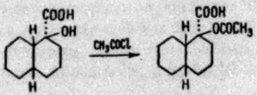
Oxidation with sodium hypobromite of the acetylalcohols (IX), (X) and (XII) yielded the stereoisomeric 1-hydroxydecalin carboxylic acids (XIII-XV).


COOH
H
OH
CH₃COCl
COOH
H
OCOCH₃
H
H

(XIII) (XVI)


COOH
H
...OH
COOH
H
...OCOCH₃
H
H

(XIV) (XVII)


COOH
H
OH
CH₃COCl
COOH
H
OCOCH₃
H
H

(XV) (XVIII)

The lower yield of the acid (XIV), in this case, can probably be explained in the same way as the great difficulties in introducing an equatorial carbon side chain into trans-1-ethynyl-1-decalol (II) and the conversion of the latter into the acetyldecal (X), which have already been discussed.

When the hydroxydecalin carboxylic acids were acetylated under mild conditions (boiling with acetyl chloride in ether [22]), only the acetates (XVI) and (XVIII) could be isolated, while the acid (XIV) was recovered unchanged without any formation of the acetate (XVII).

Considering the ease of acetylation of the hydroxyl groups in the acetylenic alcohols (III) and (V) and in the hydroxydecalin carboxylic acids (XIII) and (XV), we must assume that the hydroxyl groups in these compounds are in the equatorial position, as opposed to the hydroxyl in trans-1-ethynyl-1-decalol (II), which clearly occupies an axial position.

From a consideration of the results obtained on the rates of hydration of the isomeric ethynyldecalols (II), (III) and (V), on the abilities of the hydration products to give carbonyl group derivatives, and on the ease of oxidation of the acetyldecalols (IX), (X) and (XII) with sodium hypobromite, it is obvious that, in the compounds with axially disposed hydroxyl groups (II), (X), and (XIV), the side chains are subjected to greater steric hindrance, while in the compounds with equatorial hydroxyl groups (III), (IX) and (XIII), the side chains are less affected by steric hindrance, and these differences are probably associated with different degrees of screening by the rings.

## EXPERIMENTAL

Trans-α-decalone (I) (m.p. 32-33°) was obtained from α-naphthol by hydrogenation over a skeletal nickel catalyst at 120-130° in an autoclave, oxidation of the resulting mixture of α-decalols with sodium bichromate and 20% sulfuric acid, and isomerization of the oxidation product with powdered caustic potash. Cis-α-decalone (b.p. 82-84° at 2 mm, $n^{18.5}D$ 1.4940) was obtained by the oxidation of cis-α-decalol (m.p. 93°), which in turn was prepared by the hydrogenation of α-naphthol over a skeletal nickel catalyst at 120-130° in an autoclave, followed by freezing out from the mixture of isomeric decalols.

Infrared absorption spectra of compounds II, III, V, IX, X and XII were recorded on a double-beam infrared spectrometer IKS-2 with an NaCl prism, which gave an error in the frequency measurement of less than ± 2 $cm^{-1}$. The resolving power of the instrument was 5.8 $cm^{-1}$ in the range 800-1200 $cm^{-1}$.

Crystalline compounds were examined in carbon disulfide solution, at a concentration of $\sim 7 \cdot 10^{-2}$ M in a 1 mm cell. Liquids were examined in the pure state in a cell 0.01 mm thick.

Condensation of acetylene with trans-α-decalone (I). a) A mixture of 120 g of powdered caustic potash, 800 ml of anhydrous ether and 25 ml of ethyl alcohol was placed in a steel reactor, the air was displaced by nitrogen, and the mixture was saturated with acetylene at 20° and 6 atm pressure [12]. Then a solution of 190 g of trans-α-decalone (I) in 200 ml of ether was added with vigorous stirring over a period of 2 hours. The mixture was stirred for a further 2.5 hours at 20° and 6 atm, treated with 250 ml of water and removed from the reactor. The ether layer was separated and the aqueous layer was extracted three times with ether. The combined ethereal extracts were saturated with carbon dioxide and dried over potash. The ether was distilled off, and the residue was distilled under reduced pressure to give 178 g (80%) of a mixture of isomeric trans-1-ethynyl-1-decalols (II) and (III) in the form of a colorless liquid of b.p. 89-91° at 2 mm, $n^{19}D$ 1.5060.

b) Liquid ammonia (1 liter) was placed in a four-necked, round-bottom, 3 litre flask provided with a stirrer, a dropping funnel and gas inlet and outlet tubes, and cooled in a mixture of solid carbon dioxide and acetone to −70°. The liquid was stirred vigorously and a stream of acetylene was passed through, 28.5 g of metallic sodium was added, and the passage of dry acetylene was continued until the reaction mixture was completely decolorized (about 6 hours), after which a solution of 80 g of trans-α-decalone (I) in 400 ml of anhydrous ether was added over a period of 30-40 minutes. The acetylene stream was continued for another 12 hours, the temperature was allowed to rise gradually to −35°, and 110 g of dry ammonium chloride was added a little at a time. The greater part of the ammonia was allowed to evaporate freely, the residue was treated with 200 ml of ether and 400 ml of water, the ether layer was separated, and the aqueous layer was extracted three times with ether. The combined ether extracts were washed with 5% hydrochloric acid and then with water, and dried over sodium sulfate. The ether was distilled off and the residue was distilled under reduced pressure to give 85 g (90%) of a mixture of isomeric trans-1-ethynyl-1-decalols of b.p. 94-99° at 2 mm, $n^{17}D$ 1.5070. Petroleum ether (70 ml of b.p. 40-50°) was added, and the mixture was cooled with solid carbon dioxide to give 26.5 g of crystals of m.p. 50-52°, and these, after recrystallization from 40 ml of petroleum ether with repeated freezing out from the mother liquor, yielded 21 g of the crystalline isomer II in the form of colorless crystals.

M.p. 54-55°. $\nu$ 1032 and 1141 $cm^{-1}$.

Found %: C 80.83, 80.68; H 10.22; 10.33. $C_{12}H_{18}O$. Calculated %: C 80.84; H 10.17.

Chromatography of the mother liquor on alumina yielded 4.5 g of II and 45 g of the isomer III, in the form of a colorless liquid.

B. p. 86-87° (1 mm); $n^{20}D$ 1.5044; $d^{20}_4$ 1.0041; $MR_D$ 52.61; calc. 52.75; $\nu$ 1029, 1038, 1051, 1145 and 1156 $cm^{-1}$.

Found %: C 80.93, 81.09; H 10.21, 10.24. $C_{12}H_{18}O$. Calculated %: C 80.84; H 10.17.

The acetate of trans-1-ethynyl-decalol (VI). A solution of 15.4 g of II (m.p. 54-55°) in 35 g of freshly distilled acetic anhydride was boiled under reflux for 2.5 hours. The cooled solution was treated with 80 ml of water, and the oil was separated, taken up in ether, washed with soda solution until neutral and dried over magnesium sulfate. The solvent was distilled off, and the residue was distilled under reduced pressure to give 16.2 g (85%) of the acetate (VI) in the form of a colorless liquid.

B. p. 106-108° at 2 mm, $n^{20.5}D$ 1.4940, $d^{20}_4$ 1.0344, $MR_D$ 61.98; calc. 62.04.

Found %: C 76.51, 76.52; H 9.28, 9.23. $C_{14}H_{20}O_2$. Calculated %: C 76.32; H 9.15.

The acetate of trans-1-ethynyl-1-decalol (VII). A solution of 4 g of III (b.p. 86-87° at 1 mm; $n^{22.5}D$ 1.5033) in 8 g of freshly distilled acetic anhydride was boiled under reflux for 2.5 hours. The solution was cooled and poured into water, and the crystals deposited were separated and recrystallized from isooctane. The yield was 4.5 g (92%) of the acetate VII, of m.p. 79-80° [7].

Condensation of acetylene with cis-α-decalone (IV). Liquid ammonia (1 litre) was placed in the apparatus as described above. The liquid was stirred vigorously while a stream of dry acetylene was passed through, and 17 g of sodium, cut into small pieces, was added. When the color had completely disappeared, a solution of 50 g of cis-α-decalone (IV) in 250 ml of anhydrous ether was added, with vigorous stirring, to the suspension of sodium acetylide at − 70°, over a period of 30 minutes. The usual recovery procedure gave 42.5 g (74.3%) of a material of b.p. 88-98° at 2 mm and $n^{21.5}D$ 1.5002, from which were obtained, by dilution with petroleum ether and freezing out at − 70°, 25 g of cis-1-ethynyl-1-decalol (V) in the form of large transparent crystals.

M. p. 55-56°, $\nu$ 1022, 1037 and 1057 $cm^{-1}$.

Found %: C 80.85, 80.85; H 10.11, 10.18. $C_{12}H_{18}O$. Calculated %: C 80.84; H 10.17.

Chromatography of 17 g of the liquid residue on alumina yielded 6.8 g of V, of m.p. 56-57°, and 5.1 g of trans-α-decalone (I) of m.p. 33°. A sample of V mixed with II (m.p. 54-55°) melted at 33-35°.

The total yield of V, based on the cis-α-decalone taking part in the reaction, was 60.5%.

The acetate of cis-1-ethynyl-1-decalol (VIII). A solution of 11.7 g of V (m.p. 55-56°) in 28 g of freshly distilled acetic anhydride was boiled under reflux for 2.5 hours. The solution was cooled and poured into water, and the crystals which separated were recrystallized from isooctane. The yield was 13.2 g (90%) of the acetate VIII in the form of large, colorless, transparent crystals of m.p. 65-67°.

Found %: C 76.37, 76.21; H 9.27, 9.27. $C_{14}H_{20}O_2$. Calculated %: C 76.32; H 9.15.

Hydration of trans-1-ethynyl-1-decalol (II). A mixture of 5 g of II (m.p. 54-55°), 40 ml of methanol, 6 ml of water, 0.3 ml of concentrated sulfuric acid and 2 g of mercuric sulfate was stirred at 20° for 100 hours; the reaction's course was followed by testing samplesfor an acetylene. Under these conditions hardly any reaction took place. The reaction was only completed after boiling for 10 hours at 65°. The cooled mixture was neutralized with sodium bicarbonate solution, and the inorganic residue was filtered off. The product was extracted with ether and dried over magnesium sulfate, the ether was distilled off and the residue was distilled under reduced pressure. The yield was 3.5 g (63%) of trans-1-acetyl-1-decalol (X) in the form of a colorless liquid.

B. p. 106-107° at 2 mm, $n^{20}D$ 1.4970, $d^{20}_4$ 1.0502, $MR_D$ 54.71; calc. 54.75. $\nu$ 1029, 1045, 1082 and 1140 $cm^{-1}$.

Found %: C 73.62; 73.62; H 10.14, 10.25. $C_{12}H_{20}O_2$. Calculated %: C 73.42; H 10.27.

The semicarbazone of X was in the form of white crystals of m.p. 218-219° (from methanol).

Found %: N 16.32, 16.24. $C_{13}H_{23}O_2N_3$. Calculated %: N 16.59.

*Hydration of trans-1-ethynyl-1-decalol (III).* A mixture of 5 g of III (b.p. 86-87° at 1 mm; $n^{22.5}D$ 1.5033), 40 ml of methanol, 6 ml of water, 0.3 ml of concentrated sulfuric acid and 2 g of mercuric sulfate was stirred at 20° for 10 hours; at the end of this time a sample gave a negative test for an acetylene; metallic mercury was formed. The mixture was neutralized with dry sodium bicarbonate, the inorganic deposit was filtered off, and the product was extracted with ether and dried over magnesium sulfate. The solvent was distilled off and the residue was distilled under reduced pressure to give 4.3 g (80%) of trans-1-acetyl-1-decalol (IX), in the form of a colorless liquid.

B. p. 80-82° (1 mm), $n^{20}D$ 1.4898, $d^{20}_4$ 1.0337, $MR_D$ 54.94; calc. 54.75. $\nu$ 1060, 1097, and 1151 $cm^{-1}$.

Found %: C 73.50, 73.40; H 10.36, 10.22. $C_{12}H_{20}O_2$. Calculated %: C 73.42; H 10.27.

The semicarbazone melted at 209-210° (from methanol), and a sample mixed with the above-described semicarbazone of X (m.p. 218-219°) melted at 204-206°.

Found %: C 61.65; 61.89; H 9.14, 9.15; N 16.34, 16.59. $C_{13}H_{23}O_2N_3$. Calculated %: C 61.63; H 9.15; N 16.59.

The 2,4-dinitrophenylhydrazone of IX consisted of orange-yellow crystals of m.p. 141-142° (from ethanol).

Found %: C 51.39, 51.55; H 6.35, 6.48; N 15.09, 14.96. $C_{19}H_{24}O_5N_4$. Calculated %: C 51.43; H 6.42; N 14.88.

*Hydration of cis-1-ethynyl-1-decalol (V).* A mixture of 5 g of V (m.p. 55-56°), 40 ml of methanol, 6 ml of water, 0.3 ml of concentrated sulfuric acid and 2 g of mercuric sulfate was stirred at 20° for 70 hours. There was practically no hydration under these conditions (acetylene test). But, after the mixture had been boiled for 1 hour at 65°, mercury was deposited and the acetylene test was negative. The cooled mixture was neutralized with sodium bicarbonate solution, the inorganic deposit was filtered off, the filtrate was extracted with ether and the ethereal solution was dried over magnesium sulfate. The solvent was distilled off, and distillation of the residue under reduced pressure yielded 3.9 g (71%) of cis-1-acetyl-1-decalol (XII) in the form of a colorless liquid.

B. p. 94-96° (1 mm), $n^{20}D$ 1.5010, $d^{20}_4$ 1.0618, $MR_D$ 54.47; calc. 54.75; $\nu$ 1045, 1066, 1128 and 1150 $cm^{-1}$.

Found %: C 73.46, 73.24; H 10.33, 10.27. $C_{12}H_{20}O_2$. Calculated %: C 73.42; H 10.27.

On standing, XII crystallized completely, and was obtained in the form of colorless needles of m.p. 36.5-37° (from petroleum ether). Samples of XII, mixed with V (m.p. 55-56°), II (m.p. 54-55°) or I (m.p. 33°), melted on mixing at about 18°.

The semicarbazone of XII was in the form of colorless crystals of m.p. 203-205° (from methanol).

Found %: N 16.30, 16.43; $C_{13}H_{23}O_2N_3$. Calculated %: N 16.59.

*Hydration of the acetate of trans-1-ethynyl-1-decalol (VII).* A mixture of 3.5 g of (VII) (m.p. 79-80°), 40 ml of methanol, 5 ml of water, 0.2 ml of concentrated sulfuric acid and 1.5 g of mercuric sulfate was stirred for 4.5 hours at 65°. Metallic mercury was deposited and a sample gave a negative acetylene test. The reaction mixture was worked up in the usual way to give 2.8 g (73%) of the acetate of trans-1-acetyl-1-decalol (XI) [7] in the form of a colorless liquid.

B. p. 111-113° (1.5 mm); $n^{18}D$ 1.4880; $d^{20}_4$ 1.0752; $MR_D$ 63.63; calc. 63.99.

*Oxidation of trans-1-acetyl-1-decalol (IX) with sodium hypobromite.* A solution of sodium hypobromite was prepared from 6 g of caustic soda, 40 ml of water and 9 g of bromine. This was cooled to − 5°, 2.8 g of IX (b.p. 80-82° at 2 mm; $n^{20}D$ 1.4898) was added, and the mixture was stirred for 2.5 hours at 15°. The bromoform layer (about 4 g) was removed, the aqueous layer was thoroughly extracted with ether, and the ethereal solution was dried over magnesium sulfate. The solvent was distilled off and the residue was recrystallized from benzene. The yield was 2.5 g (89.3%) of trans-1-hydroxydecalin carboxylic acid (XIII), in the form of colorless crystals of m.p. 149-150°.

Found %: C 66.46, 66.33; H 9.10, 9.06. $C_{11}H_{18}O_3$. Calculated %: C 66.63; H 9.15.

On boiling a solution of 1 g of XIII (m.p. 149-150°) and 2.5 ml acetyl chloride in 5 ml of ether under reflux for 4 hours, a quantitative yield (1.2 g) was obtained of the acetate of trans-1-hydroxydecalin carboxylic acid (XVI) in the form of large colorless crystals of m.p. 164-165° (from benzene).

Found %: C 65.13, 64.93; H 8.40, 8.39. $C_{13}H_{20}O_4$. Calculated %: C 64.97; H 8.39.

Oxidation of trans-1-acetyl-1-decalol (X) with sodium hypobromite. Using a similar procedure, 2.8 g of X (b.p. 106-107° at 2 mm; $n^{20}D$ 1.4970) yielded 1.5 g (54%) of trans-1-hydroxydecalin carboxylic acid (XIV), in the form of colorless crystals of m.p. 115-116° (from benzene).

Found %: C 66.44, 66.56; H 9.27, 9.11. $C_{11}H_{18}O_3$. Calculated %: C 66.63; H 9.15.

Oxidation of cis-1-acetyl-1-decalol (XII) with sodium hypobromite. The bromite solution was prepared from 6.3 g of caustic soda, 40 ml of water and 9 g of bromine. This was cooled to −5°, 2.9 g of XII (b.p. 94-96° at 1 mm; $n^{20}D$ 1.5010) was added, and the mixture was stirred for 30 minutes at 0° and for 2 hours at 20°. Crystals of the sodium salt of cis-1-hydroxydecalin carboxylic acid were prepcipitated, and these were treated with dilute sulfuric acid to give 2.2 g (75%) of XV, in the form of colorless crystals of m.p. 134-136° (from benzene).

Found %: C 66.72, 66.56; H 9.22, 9.34. $C_{11}H_{18}O_3$. Calculated %: C 66.63; H 9.15.

A solution of 0.5 g of XV (m.p. 134-136°) and 1.2 ml of acetyl chloride in 2.5 ml of ether was boiled under reflux for 4 hours. The yield was 0.45 g (75%) of the acetate of cis-1-hydroxydecalin carboxylic acid (XVIII), in the form of colorless crystals of m.p. 141-142.5° (from benzene).

Found %: C 65.13, 65.10; H 8.40, 8.42. $C_{13}H_{20}O_4$. Calculated %: C 64.97; H 8.39.

## SUMMARY

We have investigated the stereochemistry of the condensation of cis- and trans-α-decalones with acetylene and some stereochemical reactions of the resulting cis- and trans-1-ethynyl-1-decalols (II), (III) and (V) and of their hydration products.

## LITERATURE CITED

[1] R. B. Wagner and J. A. Moore, J. Am. Chem. Soc. 72, 1873 (1950).

[2] J. D. Billimoria and N. F. Maclagan, J. Chem. Soc. 1951, 3067.

[3] J. R. Marshall and J. Walker, J. Chem. Soc. 1952, 467.

[4] J. D. Billimoria, J. Chem. Soc. 1953, 2626.

[5] J. D. Billimoria and N. F. Maclagan, J. Chem. Soc. 1954, 3257.

[6] G. W. Stacy and R. A. Mikulec, J. Am. Chem. Soc. 76, 524 (1954).

[7] A. E. Coles, W. H. Linnell et al., J. Chem. Soc. 1954, 2617.

[8] D. Papa, H. F. Ginsberg et al., J. Am. Chem. Soc. 76, 4441 (1954).

[9] M. C. Kloetzel and B. S. Abadir, J. Am. Chem. Soc. 77, 3823 (1955).

[10] M. C. Kloetzel and U. K. Pandit, J. Am. Chem. Soc. 78, 1412 (1956).

[11] I. N. Nazarov and A. A. Akhrem, J. Gen. Chem. 26, 1186 (1956).*

[12] I. N. Nazarov, I. L. Koltliarevskii et al., J. Gen. Chem. 23, 1900 (1953); Bull. Acad. Sci. USSR, Div. Chem. Sci. 1956, 959, 1370.*

[13] I. N. Nazarov, G. P. Verkholetova et al., J. Gen. Chem. 26, 1482 (1956).*

[14] W. Hückel, Lieb. Ann. 441, 1 (1925).

[15] I. N. Nazarov and L. D. Bergel'son, J. Gen. Chem. 22, 449 (1952).*

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*Original Russian pagination. See C.B. translation.

[16] J. English and G. Cavaglieri, J. Am. Chem. Soc. 65, 1085 (1943).

[17] D. H. R. Barton, J. Chem. Soc. 1953, 1027.

[18] D. H. R. Barton, Experientia 6, 316 (1950); J. Chem. Soc. 1951, 1048.

[19] W. Hückel, Lieb., Ann. 533, 1, 128 (1937).

[20] E. L. Eliel, Experientia 9, 91 (1953).

[21] H. Rupe and W. Messner, et. al., Helv. Chim. Acta 11, 449 (1928).

[22] J. Pascual et al., J. Chem. Soc. 1949, 1943.

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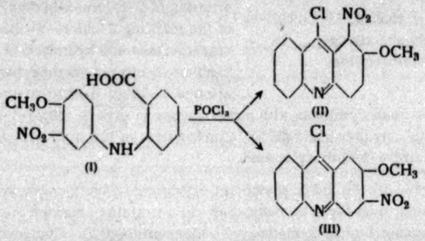
# INVESTIGATION OF ACRIDINE DERIVATIVES

## 1. SYNTHESIS OF 1-NITRO-2-METHOXY-9-CHLOROACRIDINE

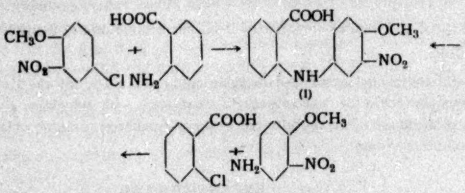
A. T. Troshchenko

Many theoretically possible acridine derivatives have not yet been prepared, in spite of their great importance for different branches of industry, and this makes it impossible to establish any general relations between them or any relationships between their properties and structures. Special methods of preparing different compounds of this class have not yet been investigated.

We were interested in the synthesis of previously unknown nitromethoxy derivatives of anthracene, in which the substituents were in the ortho position with respect to each other. One possible way of synthesizing such compounds was by the cyclization of 3'-nitro-4'-methoxydiphenylamine-2-carboxylic acid (I), which should give the two isomeric compounds – 1-nitro-2-methoxyacridine (II) and 2-methoxy-3-nitroacridine (III).



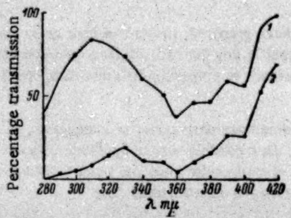
3'-Nitro-4'-methoxydiphenylamine-2-carboxylic acid was previously unknown. The synthesis of an acid of this structure could be attempted in two different ways – a) the condensation of 2-nitro-4-chloroanisole with anthranilic acid [1], and b) the condensation of 2-nitro-4-aminoanisole with o-chlorobenzoic acid.



The first of these condensations, a), was found to give the desired acid, I, but it was greatly contaminated by tarry matter, which made it difficult to purify, so that the yield was very small. We therefore tried the second method of synthesis.

The requisite 2-nitro-4-aminoanisole was prepared by the action of nitration mixture on p-acetanisidine and subsequent hydrolysis of the acetyl group [2]. The condensation of this product with o-chlorobenzoic acid gave the desired acid, I, and this had a constant melting point after a single recrystallization from glacial acetic acid. This acid could be cyclized with the aid of phosphorus oxychloride to give 2-nitromethoxy-9-chloroacridine.

This reaction could theoretically lead to the formation of the two isomeric compounds II and III, so that, after one substance had been crystallized out, the mother liquor was concentrated to yield another fraction in the form of a pure product; this second fraction was found to be identical with the first. Chromatography of the mother liquor on alumina also failed to give another product. With the object of obtaining the second possible isomer, the reaction product was subjected to stepwise hydrolysis by dilute hydrochloric acid, since it was known that the rate of hydrolysis of a chlorine atom in the 9 position is considerably affected by the nature and positions of the other substituents [3]. Two hours hydrolysis gave a product completely soluble in dichloroethane or benzene. It was only converted to an acridone after heating for 18 hours. Thus, the cyclization of I only yielded one of the possible products.



Absorption spectra (in benzyl alcohol, $10^{-4}$ cm).
1) 1-Nitro-2-methoxy-9-chloroacridine;
2) 2-methoxy-3-nitro-9-chloroacridine.

In order to establish the structure of the nitromethoxy-9-chloroacridine, we synthesized one of the possible isomers, III, by a method which excluded the possibility of isomer formation. The compound III could be obtained from a diphenylamine carboxylic acid which contained the substituents and the carboxyl group in the same ring, namely 4-methoxy-5-nitrodiphenylamine-2-carboxylic acid. This acid had not been described in the literature, but it could be synthesized by the condensation of the also undescribed 2-chloro-4-nitro-5-methoxybenzoic acid with aniline. 2-Chloro-4-nitro-5-methoxybenzoic acid was synthesized in two ways – a) by nitration of 2-chloro-5-hydroxybenzoic acid [4], methylation of the resulting 2-chloro-4-nitro-5-hydroxybenzoic acid with diazomethane and hydrolysis of the resulting methyl ester of 2-chloro-4-nitro-5-methoxybenzoic acid, and b) by methylation of 6-chloro-4-nitro-m-cresol [5] and oxidation of the resulting 6-chloro-4-nitro-3-methoxytoluene with permanganate to give 2-chloro-5-methoxybenzoic acid identical with the product of a), but in very poor yield (27%). Condensation of this acid with aniline gave a good yield of 4-methoxy-5-nitrodiphenylamine-2-carboxylic acid.

Cyclization of this acid with the aid of phosphorus oxychloride gave 2-methoxy-3-nitro-9-chloroacridine, which was found to be different from the nitromethoxy-9-chloroacridine obtained previously, and this enabled the latter to be assigned the structure 1-nitro-2-methoxy-9-chloroacridine (II). Compounds II and III had different absorption spectra.

An attempt to synthesize II from 3-nitro-4-methoxydiphenylamine-2-carboxylic acid was unsuccessful, in that we did not succeed in preparing the requisite 2-nitro-3-methoxy-6-chlorobenzoic acid, because oxidation of 2-nitro-3-methoxy-6-chlorotoluene with either permanganate or chromic mixture led to complete breakdown of the molecule.

The absorption spectra of 1-nitro-2-methoxy-9-chloroacridine and of 2-methoxy-3-nitro-9-chloroacridine were recorded (see Fig.).

3'-Nitro-4'-methoxydiphenylamine-2-carboxylic acid (acid chloride) was also subjected to cyclization by heating with phosphorus pentachloride, and subsequent treatement with anhydrous aluminum chloride. The product was a nitromethoxyacridone identical with the 1-nitro-2-methoxyacridone obtained by the hydrolysis of 1-nitro-2-methoxy-9-chloroacridine.

## EXPERIMENTAL

Preparation of 3'-nitro-4'-methoxydiphenylamine-2-carboxylic acid (I). a) Condensation of anthranilic acid with 4-chloro-2-nitroanisole. A mixture of 7.0 g of anthranilic acid, 9.4 g of 4-chloro-2-nitroanisole, 10 g of finely divided freshly calcined potash, 0.3 g of copper powder and 75 ml of nitrobenzene was heated in a round-bottom flask, under reflux, in an oil bath at 180°, for 5 hours. The nitrobenzene was distilled off in steam. The aqueous solution from the distillation flask was filtered, and the residue on the filter was extracted with hot water. The combined filtrates were made acid to congo red with dilute hydrochloric acid. The dark resinous deposit formed was washed until neutral and dried in air. It weighed 6.3 g. Three crystallizations from glacial acetic acid yielded 3.1 g (21.0%) of acid of m.p. 193-196°.

b) Condensation of o-chlorobenzoic acid with 2-nitro-4-aminoanisole. A mixture of 15.6 g of o-chlorobenzoic acid, 17.0 g of 2-nitro-4-aminoanisole 7.0 g of anhydrous potash, 0.2 g of copper powder and 30 ml of cyclohexanol was heated in a round-bottom flask, under reflux, in an oil bath at 140°, for 2 hours. The cyclohexanol was distilled off in steam, and the residue in the distillation flask was extracted with hot soda solution until it had completely dissolved. The solution was made acid to congo red with dilute hydrochloric acid. A yellow precipitate was formed. After washing and drying in air, this weighed 24 g (85%). A single recrystallization from glacial acetic acid yielded green needles of m.p. 195-197°.

Found %: C 57.54, 57.81; H 3.92, 3.95; N 9.61, 9.81. equiv. 284. $C_{14}H_{12}O_5N_2$. Calculated %: C 58.33; H 4.20; N 9.71. Equiv. 288.

Cyclization of 3'-nitro-4'-methoxydiphenylamine-2-carboxylic acid. A mixture of 28.8 g of 3'-nitro-4'-methoxydiphenylamine-2-carboxylic acid with 82 g of phosphorus oxychloride was heated in a round-bottom flask, with a reflux condenser protected by a calcium chloride tube, on a metal bath at 110-120°, for 1.5 hours. Vigorous boiling and frothing occurred at the start. At the end of this heating period the main part of the phosphorus oxychloride was distilled off under a water-pump vacuum, the residue was dissolved in 0.5 liters of chloroform, and this solution was added, with stirring, to 4 liters of 5% ammonia solution. The chloroform solution was separated and dried, and the solvent was removed. The crystalline residue weighed 29.0 g.

Recrystallization from dichloroethane yielded 18.28 g of a pale-yellow product of m.p. 195-196°. Evaporation of the mother liquor gave a further quantity of material, which, on recrystallization from dichloroethane gave the same product of m.p. 195-196°. The total yield of the pure product was 26.2 g (91%).

Found %: C 57.87; H 3.19; N 9.97. $C_{14}H_9O_3N_2Cl$. Calculated %: C 58.26; H 3.15; N 9.70.

Attempts to obtain the second of the possible isomers by crystallization of the crude product from benzene, chloroform and dichloroethane were unsuccessful. The mother liquor from the first fraction of crystals was diluted with dry dichloroethane and passed through an alumina column. Washing of the column with various solvents did not lead to any resolution of the absorption zone. Fractional elution also gave products with identical properties.

Conversion of 1-nitro-2-methoxy-9-chloroacridine into 1-nitro-2-methoxyacridone. A mixture of 0.5 g of 1-nitro-2-methoxy-9-chloroacridine and 50 ml of 1% hydrochloric acid was heated for 18 hours on a boiling water bath. The residue was filtered off, washed with water, ammonia and again with water, and dried. The resulting pale-yellow powder was insoluble in benzene, alcohol or dichloroethane. It was recrystallized from glacial acetic acid. Microscopic needles were obtained of m.p. 339°. The solution in glacial acetic acid showed an intense blue-violet fluorescence.

Production of 1-nitro-2-methoxyacridone by the cyclization of 3'-nitro-4'-methoxydiphenylamine-2-carboxylic acid in the presence of aluminum chloride. A mixture of 5.7 g of 3'-nitro-4'-methoxydiphenylamine-2-carboxylic acid, 5.0 g of phosphorus pentachloride and 50 ml of benzene was heated in a round-bottom flask to 30-40° for 30 minutes. A dark green solution was formed, from which crystals began to separate on cooling, and the cold solution was mixed with 8.0 g of finely divided anhydrous aluminum chloride. This caused the mixture to heat up, which was countered by cooling the flask in running water. The solution acquired a reddish-brown color. The mixture was shaken at intervals for 2 hours. The reaction mixture was poured into ice water, the benzene was evaporated off, and the product was washed with soda solution and with boiling water. Its weight was 5.3 g after drying. The product was recrystallized from glacial acetic acid. Microscopic yellow needles were obtained of m.p. 338°. A mixed sample, with the previously described 1-nitro-2-methoxyacridone, melted at 339°.

Found %: C 61.87; H 3.68; N 10.02. $C_{14}H_{10}O_4N_2$. Calculated %: C 62.23; H 3.74; N 10.36.

Conversion of 1-nitro-2-methoxyacridone to 1-nitro-2-methoxy-9-chloroacridine.

A mixture of 1.0 g of 1-nitro-2-methoxyacridone (obtained by cyclization in the presence of aluminum chloride) with 5.0 ml of phosphorus oxychloride was heated on a metal bath at 125-130° for 3 hours. Excess of phosphorus oxychloride was distilled off on a water bath under a water-pump vacuum. Ice and 5% ammonia were added. On shaking, the oil turned to a yellow powder, which was separated, washed and dried. The yield was 1.1 g. Recrystallization from dichloroethane gave a product of m.p. 195-196°. A mixed sample, with the product obtained by the cyclization of 3'-nitro-4'-methoxydiphenylamine-2-carboxylic acid in the presence of phosphorus oxychloride, melted at 195-196°.

Preparation of 2-chloro-4-nitro-5-hydroxybenzoic acid. A solution of 5.15 g of 3-hydroxy-6-chlorobenzoic acid in 25 ml of glacial acetic acid was kept cold while 3.2 ml of nitric acid (d 1.4) was added drop by drop, which tended to heat the mixture.

The next day the mixture was diluted with water, a pale-yellow precipitate was formed, which was separated, washed and dried. It weighed 1.13 g.

This crystallized from water in the form of fine silky needles of m.p. 147-148°.

Found %: C 38.18, 38.37; H 1.74, 1.79; N 6.0, 6.27; equiv 220. $C_7H_4O_5NCl$. Calchlated %: C 38.67; H 1.84; N 6.43. Equiv. 217.5.

Preparation of 2-chloro-4-nitro-5-methoxybenzoic acid. A solution of 1.0 g of 2-chloro-4-nitro-5-hydroxybenzoic acid in 15 ml of ether was methylated with diazomethane. The residue, after distilling off the ether and excess of diazomethane, was heated with alcoholic alkali, the alcohol was distilled off, and the residue was dissolved in water and made acid to congo red with hydrochloric acid. The organic acid was precipitated in the form of bright needles of m.p. 171-172°; weight 1.0 g.

Found %: C 41.19; H 2.50; N 5.87. Equiv. 233. $C_8H_6O_5NCl$. Calculated %: C 41.51; H 2.63; N 6.04. Equiv. 232.5.

Preparation of 2-chloro-4-nitro-5-methoxytoluene. 6-Chloro-4-nitro-m-cresol was prepared by the nitration of p-chloro-m-cresol and 13.0 g of it was suspended in 50 ml of anhydrous ether. An ethereal solution of diazomethane, prepared from 25 g of the methylnitrosamide of p-toluenesulphonic acid, was added to the suspension. There was an abundant evolution of bubbles when the diazomethane was added, and the suspended matter went into solution. On the next day the ethereal solution was washed a few times with dilute alkali and then with water. The ethereal solution was filtered through a dry filter, and the solvent was distilled off. The residue was 12.0 g of pale-yellow crystals, whose m.p. was 96-97° after recrystallization from alcohol.

Found %: C 47.12; H 3.94; N 6.21. $C_8H_8O_3NCl$. Calculated %: C 47.68; H 4.01; N 6.94.

Oxidation of 2-chloro-4-nitro-5-methoxytoluene. A mixture of 11.5 g of 2-chloro-4-nitro-5-methoxytoluene with a solution of 10 g of permanganate in 300 ml of water was placed in a flask. The mixture was stirred and boiled for 2 hours. Another 9 g of permanganate was added when the color began to fade, and the boiling was continued for another 3 hours. The solution was then colorless, but there were numerous oily drops floating on the surface and these crystallized on cooling. The treatment was continued with three further portions of 5,4 and 3 g of permanganate, but oxidation remained incomplete. Manganese dioxide and unconverted 2-chloro-4-nitro-5-methoxytoluene were filtered off. The filtrate was acidified, whereupon 3-methoxy-4-nitro-6-chlorobenzoic acid was precipitatedin the form of silky needles. The weight was 2.5 g.

Extraction of the manganese dioxide sludge with ether yielded 7 g of 2-chloro-4-nitro-5-methoxytoluene, and this was further oxidized until no more crystals were visible in the reaction mixture, this required 40 g of permanganate. The manganese dioxide was filtered off, and 1.25 g of acid was isolated, which melted at 171-172° after recrystallization from hot water. A mixed sample of this acid, with the acid obtained by the nitration of 3-hydroxy-6-chlorobenzoic acid, melted at 171-172°.

Oxidation of 2-chloro-4-nitro-5-methoxytoluene with permanganate in aqueous pyridine solution only gave traces of the acid.

Condensation of 2-chloro-4-nitro-5-methoxybenzoic acid with aniline. A mixture of 1.0 g of 2-chloro-4-nitro-5-methoxybenzoic acid, 0.7 g of freshly distilled aniline, 1.8 g of calcined potash, 0.05 g of copper powder and 15 ml of isoamyl alcohol was heated, under reflux, on a metal bath to 140-145°, for 4 hours. The solvent and excess of aniline were then distilled off in steam.

The aqueous solution was filtered and made acid to congo red with hydrochloric acid. The orange precipitate formed was washed and dried. The yield was 0.9 g. Recrystallization from alcohol gave shining orange-red leaflets of m.p. 224-226°.

Found %: C 57.89; H 3.89; N 9.81. $C_{14}H_{12}O_5N_2$. Calculated %: C 58.33; H 4.20; N 9.71.

**Preparation of 2-methoxy-3-nitro-9-chloroacridine by the cyclization of 4-methoxy-5-nitro-diphenylamine-2-carboxylic acid.** A mixture of 0.65 g of 4-methoxy-5-nitro-diphenylamine-2-carboxylic acid with 5 ml of phosphorus oxychloride was heated in a round-bottom flask, under reflux, on a metal bath at 120-130°, for 3 hours. Excess phosphorus oxychloride was distilled off on a water bath under a water-pump vacuum. Ice and 5% ammonia were added to the residue. The oil formed was converted to a yellow powder on shaking, and this was separated, washed and dried. The yield was 0.6 g. Recrystallization from dichloroethane gave green-yellow, needle-shaped crystals, of m.p. 205-206°, darker than crystals of 1-nitro-2-methoxy-9-chloroacridine.

Found %: C 57.91; H 3.21; N 9.46. $C_{14}H_9O_3N_2Cl$. Calculated %: C 58.26; H 3.15; N 9.70.

## SUMMARY

1. The previously unknown 3'-nitro-4'-methoxydiphenylamine-2-carboxylic acid has been synthesized.

2. It has been shown that only one of the possible isomers – 1-nitro-2-methoxy-9-chloroacridine – is formed by the cyclization of 3'-nitro-4'-methoxydiphenylamine-2-carboxylic acid with phosphorus oxychloride.

3. In the course of demonstrating the structure of this isomer, the previously unknown 4-methoxy-5-nitro-diphenylamine-2-carboxylic acid has been synthesized and converted into 2-methoxy-3-nitro-9-chloroacridine.

## LITERATURE CITED

[1] A. I. Kiprianov and P. I. Mikhailenko, Ukraine Chem. J., 5, 226 (1930).

[2] German Patent 101778; Zbl., 1899, I, 1175; M. Heidelberg, and W. Jacobs, J. Am., Chem. Soc., 41, 1450 (1919).

[3] Linnel and Stuckey, Quart. J. Pharm. Pharmacol., 13, 162 (1940).

[4] V. I. Minaev, J. Russ. Chem. Soc., 58, 113 (1926); Beyer, Rec. trav. Chim., 40, 627 (1921).

[5] Walter, Zipper, J. pr. Ch., 91, 411 (1915).

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# ORIENTATION IN SUBSTITUTION IN THE AROMATIC NUCLEUS

## IV. SULFONATION OF CHLOROBENZENE

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Chlorobenzene was first sulfonated with fuming sulfuric acid in 1857 [1]. The product was p-chlorobenzenesulfonic acid, but, later, the formation of bis-(4-chlorophenyl)sulfone was also observed [2]. In the next 100 years, the sulfonation of chlorobenzene, by different sulfonating agents under various conditions, was the subject of a number of investigations [3-8]. No other products than p-chlorobenzenesulfonic acid were ever obtained, and this work was the basis for Holleman's [9] statement that sulfonation of chlorobenzene gave 100% of p-isomer and that the m- and o-isomers were completely absent in the sulfonation product. The results quoted in these references are quite definite, but the authors did not investigate all possible conditions of sulfonation.

But, considering some of the rules for the orientation of substituents in the benzene nucleus, it would appear that the formation of the ortho isomer should be possible by direct sulfonation, and that the formation of the meta isomer should not be impossible under certain conditions. The meta isomer is the most resistant to the reverse reaction of desulfonation [10], and its formation during sulfonation occurs at a very low rate because of the high value of the activation energy for substitution in the meta position [11]. The amount of the stable isomer formed should increase with the activity of the sulfonating agent and with increasing temperature of reaction [12]. Proceeding from this basis, we were able to demonstrate the formation of both o- and m-chlorobenzenesulfonic acids by the direct sulfonation of chlorobenzene, which was the object of this investigation.

To investigate the possibility of forming the ortho isomer, we sulfonated chlorobenzene with 100% sulfuric acid at room temperature. From the resulting sulfonic acid we obtained a sulfonyl chloride with a setting point of 52.5°, which, according to the thermal curve [13], corresponds to a para isomer content of 99.4%. Sulfonation with chlorosulfonic acid at −15° gave a sulfonyl chloride with the same setting point. Believing that the obstacle to the formation of the ortho isomer might be steric hindrance, caused by the large size of the sulfonating forms $HSO_3^+$ or $H_3SO_3^+$, we investigated the sulfonation of chlorobenzene with sulfuric anhydride in dichloroethane at low temperatures. The results of these experiments, given in Table 1, showed that sulfonation with sulfuric anhydride did give a mixed product, the content of the ortho isomer increasing with decreasing temperature.

o-Chlorobenzenesulfonyl chloride was isolated from the product of the last experiment, using their arylamine salts to separate the isomers.

It thus appears that there is considerable steric hindrance to the formation of the ortho isomer, and that the sulfonating form of sulfuric anhydride differs in volume from the sulfonating forms of sulfuric acid and chlorosulfonic acid.

In order to investigate the possibility of the formation of the meta isomer, chlorobenzene was sulfonated with sulfuric acid at temperatures from 150 to 238°. The experimental results given in Table 2 showed that formation of m-chlorobenzenesulfonic acid began at 150° or at a slightly higher temperature. The amount formed increased with rise in temperature and with duration of the reaction. The meta isomer was not formed in analytically detectable quantity in the primary process of sulfonation at low temperatures. At 150° and above, the quantity of the meta isomer increased, not only by its formation in the primary process, but also as the result of isomerization of sulfonic acid, the latter process being favored by the greater stability of the meta isomer towards desulfonation [10]. It appears that a condition approaching equilibrium between the isomers was achieved after 20 hours at 238°. The ortho isomer was absent from all the mixtures of Table 2. The para and

TABLE 1

Sulfonation of Chlorobenzene in Dichloroethane with Sulfuric Anhydride

| Sulfonation temperature | Setting point of the acid chloride obtained | Content of ortho isomer according to thermal curve (%) | Formation of sulfone (as % of sulfonic acid) |
|---|---|---|---|
| −12° | 50.2° | 5.8 | 3.4 |
| −5 to 0 | 51.4 | 3.2 | 5.3 |
| −0 to + 5 | 52.0 | 1.8 | – |

meta isomers formed were separated by making use of the solubility differences of some of their arylamine salts.

Thus, more than 50% of meta isomer was obtained by sulfonating chlorobenzene for 12-15 hours at 238°. There was a change in orientation even at relatively low temperatures, principally due to isomerization, a factor which restricts the application of the classical rules of substitution in the benzene nucleus.

## EXPERIMENTAL

Sulfonation of chlorobenzene. The sulfonation of chlorobenzene at low temperatures was carried out in a three-necked flask, fitted with a stirrer and a thermometer. Chlorobenzene (5.63 g) was dissolved in 20 ml of dichloroethane and kept at −12°, while 4.5 g of sulfuric anhydride vapor was introduced through a tube leading into the solution, over a period of 2 hours.

TABLE 2

Sulfonation of Chlorobenzene with 100% Sulfuric Acid.

| Reaction temperature | Duration (in hours) | Chlorobenzene used (mole per mole $H_2SO_4$) | Concentration of sulfuric acid used in mixture (%) | Chlorobenzene sulfonated (% of taken) | Sulfone formed (in mole % of chlorobenzene sulfonated) | Setting point of mixture of sulfonyl chlorides | Amount of meta isomer (% of total sulfonic acids) | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | thermal analysis | amination and bromination |
| 150° | 10 | 0.762 | 78.0 | | | 52.4° | 0.6 | |
| 170 | 10 | 0.795 | 76.8 | | | 51.6 | 2.8 | |
| 183.5 | 10 | 0.751 | 78.2 | | | 49.5 | 7.3 | 7.0 |
| 202.5 | 10 | 0.760 | 79.3 | | | 47.9 | 10.4 | 10.4 |
| 220 | 10 | 0.796 | 78.0 | 79.5 | 2.4 | 41.0 | 23.5 | |
| 220 | 20 | 0.796 | 77.8 | 78.0 | 4.7 | 33.9 | 35.4 | 35.5 |
| 220 | 40 | 0.796 | 77.7 | 78.1 | 4.8 | 27.2 | 45.5 | |
| 238 | 5 | 0.754 | 76.5 | 83.6 | 5.6 | 33.2 | 36.5 | |
| 238 | 10 | 0.754 | 76.0 | 84.8 | 7.1 | 25.6 | 47.6 | 47.5 |
| 237 | 20 | 0.703 | 77.5 | 86.5 | 6.4 | | | |
| 238 | 20 | 0.754 | 75.7 | 85.5 | 7.5 | 20.0 | 55.1 | |
| 238 | 34.5 | 0.754 | 74.2 | 87.9 | 7.3 | 19.7 | 55.5 | |

The mixture was maintained at − 11° for 20 hours and then poured into water, the solution was neutralized with soda, and the dichloroethane layer was separated. Evaporation of the dichloroethane yielded 0.34 g of sulfone. The aqueous solution was evaporated to dryness, and phosphorus pentachloride was used to convert the salt into the acid chloride, which melted at 50.2° after distillation.

In order to isolate the ortho isomer, the aqueous solution of the sulfonate from the last experiment (see Table 1), in which 56.2 g of chlorobenzene was sulfonated, was treated with a hot saturated solution of 75 g of phenylhydrazine hydrochloride. The salt of the para isomer (81.6%) separated on cooling, and still more of this salt was deposited when the filtrate was concentrated to a volume of 150 ml. The filtrate was neutralized, the phenylhydrazine was extracted with ether, and the solution was treated with a saturated solution of 4.5 g of o-dianisidine hydrochloride. The solution was concentrated to 50 ml and cooled to 0°, when the o-dianisidine salt of the ortho isomer was precipitated. This salt was decomposed with alkali, the amine was extracted with ether, and the resulting alkali salt was used to form a fresh precipitate of the o-dianisidine salt. This was again decomposed with alkali, and from it was obtained 0.5 g of the acid chloride of setting point 24°. Admixture with a pure sample of the ortho acid chloride gave no depression.

TABLE 3

Formation of Precipitate on Addition of the Stated Volume of a Solution of the Sodium Sulfonate to 10 ml of a Solution of Amine Hydrochloride

| Solution of hydrochloride | Normality | 0.05 N solutions of the respective isomeric sodium chlorobenzene sulfonates (ml) | | |
|---|---|---|---|---|
| | | ortho | meta | para |
| Aniline | 0.5 | 14 (no ppt.). | 14 (no ppt.) | 14 (no ppt.) |
| o-Toluidine | 0.5 | 11 (no ppt.) | 14 (no ppt.) | 14 (no ppt.) |
| m-Toluidine | 0.5 | 2.4 | 14 (no ppt.) | 14 (no ppt.) |
| m-4-Xylidine | 0.5 | 2.0, 0.6 (0°) | 14 (no ppt.) | 14 (no ppt.) |
| Pseudocumidine | 0.5 | 0.75 | 0.92 | 1.5 |
| o-Anisidine | 0.5 | 11 (no ppt.) | 14 (no ppt.) | 5 (no ppt.) |
| p-Anisidine | 0.5 | 14 (no ppt.) | 12 (no ppt.) | 12 (no ppt. |
| Benzidine | Saturated solution | 2.0 | 0.7 | 0.45 |
| o-Toluidine | The same | 2.0 | 6.0 | 4.5 |
| o-Dianisidine | 0.2 | 2.0 | 14 (no ppt.) | 14 (no ppt.) |
| 1-Naphthylamine | 0.2 | 1.0 | 1.5 | 1.5 |
| 2-Naphthylamine | 0.18 | 0.6 | 0.4 | 0.03 |
| Benzylisothiourea | 0.5 | 1.0 | 0.7 | 0.5 |
| m-Nitroaniline | Saturated solution in 2 N HCl | 6.0 | 4.0 | 4.5 |
| p-Nitro-o-toluidine | | 10 (no ppt.) | 2.5 | 0.55 |
| m-Nitro-o-anisidine | | 3.0, 0.5 (0°) | 14 (no ppt.) | 13 |
| Phenylhydrazine | 0.5 | 14 (no ppt.) | 2.0 | 0.03 |
| p-Aminoacetophenone | 0.5 | 14 (no ppt.) | 10 (no ppt.) | 14 (no ppt.) |

The sulfonation of chlorobenzene at high temperatures (see Table 2) was carried out with 100% sulfuric acid in sealed tubes, heated in a thermostat controlled to within ± 0.5° of the stated temperature. At 238° the variation was ± 1°. The sulfonation product was analyzed by the method previously described [13]. Since the ortho isomer was not formed at high temperatures, in a number of the experiments we only made use of the thermal method of analysis.

Use was made of the difference in solubilities of the phenylhydrazine and pseudocumidine salts of the para and meta isomers in order to isolate the meta isomer from the sulfonation product. The product, from the sulfonation of 15 g of chlorobenzene for 20 hours at 238°, was poured into water and neutralized with barium carbonate, with addition of soda to form the sodium sulfonate. The barium sulfate was separated off, the solution was concentrated to 88 ml and brought to the boil, and 6.7 g of phenylhydrazine hydrochloride was added. After standing overnight, the salt of the para isomer was filtered off, and the filtrate was treated with a solution of 7 g of pseudocumidine hydrochloride (the total volume of the solution was 325 ml). After 2 hours, the salt precipitated was filtered off, washed and decomposed with alkali solution. The amine was extracted with ether, the aqueous solution was evaporated to dryness to give 5.44 g (~ 45%) of the sodium salt, and this was converted by $PCl_5$ to 4.48 g of m-chlorobenzenesulfonyl chloride of setting point 23.5°, which, according to the thermal curve [13], corresponded to 94.8% of meta isomer. Admixture with a sample of the pure m-chloride gave no change in the setting point.

The sulfonation products of the last two experiments (Table 2) were checked for the presence of disulfonate. Thus, the barium content was determined for the barium salt, obtained from the acid chloride isolated in the penultimate experiment. The chloride from the last experiment was hydrolyzed with water in pyridine solution, and the total acid was titrated with 0.1 N alkali in order to calculate the molecular weight. The chlorine in the solution was determined gravimetrically.

Found %: Ba 26.44; Cl 16.76. M 210.6. $C_{12}H_8O_6S_2Cl_2Ba$. Calculated %: Ba 26.39; Cl 16.81. M 211.0.

The quantity of sulfone formed increased with rising temperature and duration of sulfonation. We set out to reduce the sulfone formation in an experiment at 237° by reducing the amount of chlorobenzene taken to 0.7 mole per mole of acid. The sulfone content of the product was then reduced to 1%.

*Arylamine salts.* Semiquantitative measurements were made on the solubilities of the salts of the different chlorobenzene sulfonic acids with 18 amines, with a view to their possible use for determining the isomers. A 0.05 N solution of the sodium sulfonate was run slowly from a buret into 10 ml of an aqueous solution of the amine hydrochloride, until a precipitate was formed. Stirring with a glass rod was used to prevent the formation of supersaturated solutions. A precipitate of the amine salt was formed when the stated quantity (in ml) of the sodium sulfonate solution had been added. Readily soluble salts did not precipitate when a considerable quantity of the sodium sulfonate had been added. The results, shown in Table 3, gave an estimate of the solubilities of the salts in the presence of excess of amine hydrochloride, and also indicated which amines were suitable for isolating the isomeric chlorobenzenesulfonic acids.

Thus 2-naphthylamine could be used for precipitating all three isomers. We used phenylhydrazine to separate the para from the ortho isomer, and the latter was isolated by means of m-4-xylidine, but quantitative separation of the isomers by means of their arylamine salts was incomplete.

## SUMMARY

1. For the first time, 1.8-5.8% of o-chlorobenzenesulfonic acid has been obtained by the sulfonation of chlorobenzene, using sulfuric anhydride at − 12 to + 3°.

2. The formation of m-chlorobenzenesulfonic acid has also been observed for the first time in the sulfonation of chlorobenzene, at temperatures from 150 to 238°, the quantity formed increasing to a limiting value with increasing temperature and time of reaction. Sulfonation with sulfuric acid at 238°, for 12-15 hours, gave a mixture of chlorobenzenesulfonic acids containing 50% of the meta isomer. The ortho isomer was not formed at these high temperatures.

3. The change in the ratio of the isomers observed at high temperatures restricts the application of the classical rules of substitution in the benzene nucleus.

4. Semiquantitative determinations have been made of the solubilities of the salts of the o-, m- and p-chlorobenzene sulfonic acids with 18 amines.

## LITERATURE CITED

[1] L. Hutchings, J. pr. Ch., 73, 60 (1858).

[2] R. Otto, Lieb. Ann., 145, 29 (1868).

[3] R. R. Baxter and F. Chattaway, J. Chem. Soc., 107, 1815 (1915).

[4] Ch. Courtot and J. Bonnet, C. r., 182, 856 (1926).

[5] E. Gilbert et. al, Ind. Eng. Ch., 45, 2065 (1953).

[6] USA Patent 2593001 (1952).

[7] I. Tanasescu and M. Macarovici, Bull. Soc. Chim., (5), 5, 1126 (1938).

[8] A. M. Grigorovskii, N. N. Dykhanov and Z. M. Kimen, J. Appl. Chem., 28, 616 (1955).*

---

*Original Russian pagination. See C.B. translation.

[9] A. F. Holleman, Chm. Revs., 1, 187 (1924).

[10] A. A. Spryskov and N. A. Ovsiankina, J. Gen. Chem. 24, 1810 (1954).*

[11] W. W. Jones and M. Russell, J. Chem. Soc., 1947, 921.

[12] A. A. Spryskov, and T. I. Iakovleva, J. Gen. Chem., 27, 239 (1957).*

[13] A. A. Spryskov, and O. I. Kachurin, J. Gen. Chem. 27, 3072 (1957).*

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* Original Russian pagination. See C.B. translation.

# THE STUDY OF CHITIN

## III. HYDROXYETHYL AND ETHYL ETHERS OF CHITIN

S. N. Danilov and E. A. Plisko

We have noted previously that the formation of chitin ethers is difficult because chitin swells very weakly in alkaline solutions [1]. A study of its heat of swelling in caustic soda solutions [2] showed that the interaction of chitin with alkali is difficult.

Preliminary experiments on the formation of hydroxyethyl esters of chitin showed that these were not produced under the conditions used for the synthesis of hydroxyethyl ethers of cellulose. The conditions for ether formation and for activation with alkali were changed; the chitin was processed with alkali solution with freezing. Etherification was carried out at higher temperature and for a longer time. Chitin of a different particle size was also used for the etherification, and the mole ratio of chitin to ethylene oxide was altered. Hydroxyethyl ethers with a high degree of etherification and which were soluble in aqueous caustic soda and in water were obtained.

The ethylation of the alkali derivative of chitin was carried out with ethyl chloride in sealed tubes and in an autoclave. Temperature conditions were established which gave chitin ethyl ethers with a degree of substitution of about 1.5, and these were soluble in organic solvents, did not swell in water and formed films with good mechanical properties.

## EXPERIMENTAL

### 1. Hydroxyethyl Ethers of Chitin

Pulverized chitin, obtained from crab shells [3], was used for the synthesis in the form of its alkali derivative, and this was treated with twice the theoretical quantity of ethylene oxide (b.p. 14° at 747 mm). Conditions were established which gave hydroxyethyl ethers soluble in water, in dilute alkali and in dilute acetic and formic acids.

Some of the more characteristic experiments have been selected from a large number of syntheses in which the particle size of the chitin was varied from 1 to 3 mm, the concentration of alkali from 20 to 43%, the mercerization temperature from room temperature to − 70°, the etherification temperature between 16, 30, 50 and 70° and the duration between 10, 20 and 30 hours.

a) Chitin (6.8 g of sample 2, Table 1) was passed through a 1 mm sieve, placed in a 150 ml flask and treated with 100 ml of 43% aqueous caustic soda. The flask was stoppered, placed in solid carbon dioxide in a Dewar flask for 20 minutes, and then allowed to stand at room temperature for 1 hour. The cooling operation was repeated three times. The swollen alkali derivative of chitin obtained was squeezed out to a third of its weight, disintegrated and heated in an autoclave, with a solution of 13.4 ml of ethylene oxide in 30 ml of acetone, for 15 hours at 50°, after which the second half of the ethylene oxide was added, and the mixture was again heated for 15 hours at the same temperature.

After this 30 hours heating at 50°, with a mole ratio of chitin to ethylene oxide of 1 : 16, the product was yellow and very viscous. Strong swelling and partial dissolution made it difficult to free the chitin hydroxyethyl ether from alkali and secondary products by washing with water on a filter, so it was electrodialyzed until there was no further reaction for alkali in the cathodic compartment. The ether was then separated from the solution by addition of acetone, which precipitated it in the form of a white voluminous mass. The product was washed three or four times with acetone by decantation, transferred to a filter, washed with ether and dried in a vacuum dessicator without heating (yield 6.2 g).

After drying, the product swelled less than beforehand in water, dilute alkali and dilute acetic and formic acids. The use of a lower concentration of mercerizing alkali (19.5%), and four coolings to − 40°, gave an ether (sample 1, Table 1) with a lower degree of substitution.

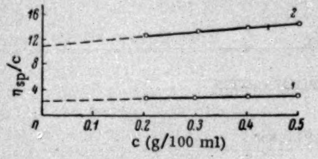

Fig. 1. Viscosity concentration curves for solutions of the hydroxyethyl ether of chitin. 1) In water; 2) in 2.26% acetic acid.

In other experiments (sample 3, Table 1), the alkali derivative of chitin was treated with ethylene oxide in benzene solution, for 30 hours at 70°, with a mole ratio of chitin to ethylene oxide of 1 : 16. The reaction product was a slightly yellow, pasty mass. The benzene was removed, and the product, which swelled and dissolved in water, was allowed to stand. It was purified by dialysis, or electrodialysis, and separated from the solution by addition of acetone. A freshly precipitated sample (before drying) dissolved readily in water, 4-8% aqueous caustic soda, 3% acetic and oxalic acids, and 40-50% phosphoric acid; it could be precipitated from these solutions by acetone. After drying in a vacuum desiccator, the product swelled strongly in the above solvents.

It was established that the best conditions for synthesizing water-soluble hydroxyethyl chitin ethers were as follows – mercerization with 43% caustic soda, cooling 1 to 3 times to low temperatures, a squeezing coefficient of about 3, an etherification temperature of + 70°, a time of 30 hours, 16 mole of ethylene oxide to 1 of chitin and a chitin particle size of 1 mm. Other conditions gave ethers which only swelled in water or dilute alkali, or did not even swell. The slightly broken down and etherified products dissolved like chitin in 60% sulfuric, 78% phosphoric and 50% nitric acids. The more highly etherified chitin ethers dissolved in 4-8% caustic soda, in water and in dilute acetic acid.

Some of the samples were analyzed for C, H and N, and their formulae were calculated. Analyses of samples 1, 2 and 3 are shown in Table 1.

TABLE 1

Analyses of Hydroxyethyl Ethers of Chitin

| Expt. No. | Content (%) | | | | Composition | Number of $CH_2CH_2OH$ groups |
|---|---|---|---|---|---|---|
| | C | H | N | $CH_3CO$ | | |
| 1 | 48.72 | 7.19 | 5.20 | 12.65 | $C_{10.9}H_{19.4}O_{6.5}$ | 1.44 |
| 2 | 49.21 | 7.49 | 5.00 | — | $C_{11.7}H_{21.4}O_{6.8}$ | 1.74 |
| 3 | 50.12 | 8.14 | 3.92 | 5.50 | $C_{14.8}H_{29}O_{8.4}$ | 2.93 |

Sample 1 was nitrated, with a nitration mixture containing 24.86% $HNO_3$, 71.55% $H_2SO_4$ and 3.59% $H_2O$, for 2 hours at 23-24°. The product contained 5.71% of nitrogen (Lunge), which corresponded to 1.34 hydroxyl groups (see Table 1).

Fig. 1 shows the intrinsic viscosity of chitin hydroxyethyl ether (sample 3) in water and in 2.26% acetic acid. It is apparent that the intrinsic viscosity is nearly five times as great in acetic acid as in water, while the slopes of the curves, characteristic of the interaction of solvent with solute, are almost the same.

## 2. Ethyl Ethers of Chitin

We obtained the previously unknown chitin ethyl ethers by the action of ethyl chloride on the alkali derivative of chitin. The latter was obtained by treating chitin with two lots of concentrated alkali solution for 20-30 minutes at room temperature. The product obtained was either allowed to mature at room temperature for 24 hours or ethylated at once. Ethylation was first carried out in glass ampules, which were charged with the alkali derivative of chitin and cooled before adding ethyl chloride mixed with benzene (75% of the amount of ethyl chloride). The ampules were then sealed and placed in a thermostat for heating to the requisite temperature.

Preliminary experiments showed that ethylation was incomplete after 10 hours at 100-120°, and that the main product was weakly ethylated and swelled in alcohol. Raising the ethylation temperature to 130° and reducing the time of reaction to 5 hours did not lead to any improvement in the solubility of the product in organic solvents.

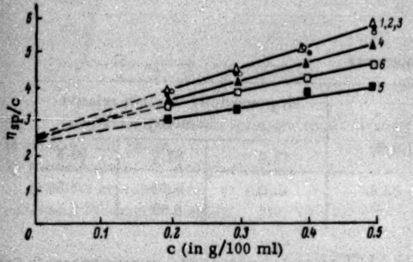

Fig. 2. Effect of solvent on the slope of the curve and on the intrinsic viscosity.
1) o-Xylene; 2) benzene; 3) toluene; 4) methylethyl ketone; 5) 1 : 4 mixture of alcohol and benzene; 6) chloroform.

In subsequent experiments the time of reaction was increased to 10 hours, and the temperature was controlled as follows: 1 hour up to 60°, 1 hour up to 80°, 1 hour up to 130° and 7 hours at 130°. Products with a higher ethoxy content were obtained in this way, and their solubility in organic solvents was considerably increased. But ethylation in ampules gave very heterogeneous products, because the ampules were not stirred, and formation of a film of ethylated chitin on the surface of the chitin macromolecule retarded the diffusion of ethyl chloride into the interior of the macromolecule. Ethylation took place much better in an autoclave with a rotating stirrer under the same conditions as above.

The products obtained were almost completely soluble in organic solvents. The isolation and purification of the ethylated chitin was carried out by a method similar to that used for the purification of ethylcellulose [4]. A difference between ethylchitin and ethylcellulose was that the former did not melt, but began to decompose at 180-190° in the presence of air, and at 200-210° in vacuo.

A full analysis was carried out on a selected sample for C, H, N, $C_2H_5O$-, $CH_3CO$- and -OH. Free hydroxyl was also determined by the Van Slyke method, since, under the conditions of the reaction, acetyl groups could split off from nitrogen.

TABLE 2

Analysis of Ethylated Chitin

| Content (%) | | | | | | |
|---|---|---|---|---|---|---|
| C | H | N | $C_2H_5O$ | $CH_3CO$ | OH | $NH_2$ |
| 54.98 | 9.22 | 6.19 | 33.83 | 4.53 | 2.75 | 2.04 |

Table 2 shows the analysis of the sample, obtained from chitin which had been mercerized with 50% caustic soda for half an hour. Ethylation was carried out in an autoclave, in the presence of 16 mole of caustic soda and 15 mole of ethyl chloride for each mole of chitin, over a period of 10 hours and a temperature range of 60 to 130°.

On the basis of this analysis the sample had the composition $C_{9.6}H_{17.53}N_{0.91}O_{4.14}$ and the formula

$$[C_6H_7O_2(OH)_{0.34}(NH_2)_{0.70}(NHCOCH_3)_{0.21}(OC_2H_5)_{1.50}]_n.$$

Measurements of viscosity were carried out on this sample in dilute solution in o-xylene, benzene, toluene, methylethyl ketone, chloroform and a 1 : 4 mixture of alcohol and benzene, at 20°, using an Ubbelohde suspended level viscometer [5].

The results are shown in Fig. 2, from which it appears that the intrinsic viscosity in the different solvents varies between 2.3 and 2.6. The viscosity curves have different slopes which are characteristic of the interaction between solvent and solute, i.e., the solvent power of the solvent. According to the data of Spurlin [6] and Alfrey [7], a steep slope corresponds to a bad solvent. So in our case the best solvent was the 1 : 4 mixture of alcohol and benzene.

The molecular weight of the sample of Table 2 was determined in methylethyl ketone by sedimentation in an ultracentrifuge,* and was found to be 66,000.

TABLE 3

Hygroscopicity of Ethylchitin after 24 Hours at Room Temperature

| No. | Sample | Ethoxyl (in %) | Hygroscopicity in air of relative humidity | | |
|---|---|---|---|---|---|
| | | | 42.0 | 62.0 | 96.5 |
| 1 | Ethylchitin. . . . . . . . . . . . . . . . . . | 33.83 | 0.51 | 2.05 | 5.55 |
| 2 | Ethylcellulose grade NI. . . . . . . . . | – | – | 0.79 | 2.54 |

Ethylated chitin differed from ethylcellulose in that it was quite highly hygroscopic, as may be seen in Table 3. The hygroscopicity evidently increased because of the partial removal of acetyl from the acetamide groupings.

Ethylated chitin, containing 33.83% of ethoxyl, dissolved in various organic solvents, and gave clear 5% solutions in alcohols (methyl, ethyl, butyl, isobutyl, hexyl, cyclohexyl, benzyl), ketones (acetone, cyclhexanone, methylethyl ketone), halogen derivatives (chloroform), esters (diethyl and dibutyl phosphates, butyl acetate, isoamyl acetate), and in benzene, toluene, xylene and their 20% mixtures with alcohol.

TABLE 4

Properties of Ethylchitin Films

| No. of sample | Tensile strength (kg/ mm$^2$) | Extension at rupture (%) | [$\eta$] | Dielectric constant |
|---|---|---|---|---|
| 1 | 6.8-7.3 | 15.1-22.8 | 2.30 | E 3.20 at $f$ 10$^3$ and tan $\delta$ 4.66 · 10$^{-3}$ |
| 2 | 6.4-7.1 | 23.0-23.9 | 1.40 | |
| 3 | 5.5-5.9 | 5.1-8.1 | 1.73 | |

The viscosity of a 5% solution in a 1 : 4 mixture of alcohol and benzene at 20° was 484 centipoises.

A film was cast from a concentrated solution (5-8%) of ethylchitin in alcohol - benzene mixture. The solution had previously been filtered under pressure through a No. 1 Schott filter. The film was cast on a carefully cleaned glass surface. After the solvent had evaporated, the film was allowed to dry in air before drying out at 60-80° in a vacuum desiccator for 5-6 days. The films were tested for yield strength and extension (Table 4). Samples did not soften on heating.

It appears from Table 4 that the tensile strength varied between 5.5 and 7.3 kg/ mm$^2$ and the extension between 5 and 23%. Films, made from ethylated chitin prepared in ampules, showed a lower tensile stength and a lower extension, since under these conditions there was a greater degradation of the alkali derivative of chitin (see intrinsic viscosity). Fig. 3 shows comparative load - extension curves for derivatives of cellulose and ethylated chitin. It is clear from the diagram that films of nitrocellulose and acetylcellulose have higher tensile strengths than those of ethylcellulose and ethylchitin, but that the former have much lower extensions. Ethylated chitin films dye well with wool dyestuffs.

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* Our thanks are due to S. Ia. Frenkel' for this determination.

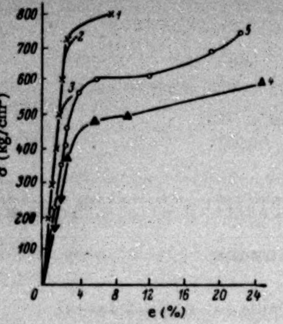

Fig. 3. Load extension curves for derivatives of cellulose and chitin.
1) Nitrocellulose; 2) acetylcellulose; 3) cellulose acetobutyrate; 4) ethylcellulose; 5) ethylated chitin.

## SUMMARY

1. The degree of etherification and the solubility of hydroxyethyl ethers of chitin are affected by the temperature, the mole ratio of the reagents, the time of reaction, the conditions for the preparation of the alkali derivative of chitin and also by the state of division of the chitin.

2. The ethyl ethers of chitin, produced for the first time, are soluble in alcohols, ketones, hydrocarbons, esters and mixed solvents.

Ethylchitin films are not as strong as those made of ethylcellulose, but show somewhat greater extension.

## LITERATURE CITED

[1] S.N. Danilov and E.A. Plisko, J. Gen. Chem. 24, 1761 (1954).*

[2] N. Il Klenkova and E. A. Plisko, J. Gen. Chem. 27, 399 (1957).*

[3] S. N. Danilov and E. A. Plisko, J. Gen. Chem. 24, 2071 (1954).*

[4] S. N. Ushakov, "Cellulose Ether and Derived Plastics," Khimizdat (1941).

[5] M. P. Volarovich, Zav. Labs. 11, 49 (1945).

[6] Spurlin, J. Polymer Sci. 1, 63 (1946).

[7] Alfrey, J. Coll. Sci. 2, 99 (1947).

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# INVESTIGATION IN THE FIELD OF COMPOUNDS LABELLED WITH $C^{14}$ AND $N^{15}$

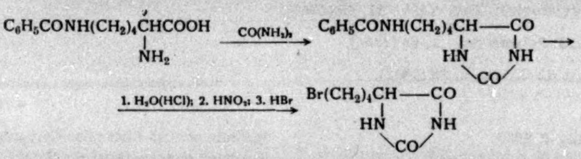
## IX. SYNTHESIS OF $\omega$-$N^{15}$-AMINO ACIDS *

V. I. Maimind, O. M. Enisherlova, K. M. Ermolaev, R. G. Vdovina,
G. A. Galegov and M. M. Shemiakin

We have previously described [2] the conditions for preparing various $\alpha$-$N^{15}$-amino acids by the phthalimide method, and shown that the yield of the final labelled compound was usually 75-95%, based on potassium phthalimide-$N^{15}$, which in turn was obtained from $N^{15}H_3$ in practically quantitative yield [3]. Further investigation showed that the phthalimide method was quite applicable to the synthesis of $\omega$-$N^{15}$-amino acids. In this paper we present the results of an investigation of the synthesis, by this means, of $\epsilon$-$N^{15}$-lysine and $\delta$-$N^{15}$-ornithine.

$\epsilon$-$N^{15}$-Lysine. There is only one method described in the literature for preparing $\epsilon$-$N^{15}$-lysine [4], according to which $\delta$-bromobutylphthaloylaminomalonic ester is condensed with potassium phthalimide-$N^{15}$, and the resulting diphthaloyl dervative is hydrolyzed with HCl; the yield of lysine dihydrochloride amounts to about 50%.

We tried to carry out the synthesis of $\epsilon$-$N^{15}$-lysine by the condensation of potassium phthalimide-$N^{15}$ with 5-( $\delta$-bromobutyl)-hydrantoin [5], which was obtained from unlabelled $\epsilon$-N-benzoyllysine as follows:


$C_6H_5CONH(CH_2)_4CHCOOH$
$NH_2$
$CO(NH_2)_2$
$C_6H_5CONH(CH_2)_4CH$—CO
HN NH
CO
1. $H_2O(HCl)$; 2. $HNO_2$; 3. HBr
$Br(CH_2)_4CH$—CO
HN NH
CO

All the stages of this synthesis proceeded satisfactorily, except for the diazotization, where the yield of hydroxybutylhydratoin did not exceed 25%. The condensation of potassium phthalimide-$N^{15}$ with bromobutylhydantoin and the subsequent hydrolysis of the phthaloyl derivative gave $\epsilon$-$N^{15}$-lysine in 50% yield. But a determination of the isotopic composition of the nitrogen in the lysine obtained (see Table) showed that it contained only about half the expected amount of $N^{15}$. This dilution of the marker was associated with the fact that, even before the condensation, the potassium of the potassium phthalimide-$N^{15}$ distributed itself approximately equally between the NH group of phthalimide and the equally acid 3-NH group of 5-( $\delta$-bromobutyl)-hydantoin. The result was that the latter condensed to an approximately equal extent with potassium phthalimide-$N^{15}$ and with potassium 5-( $\delta$-bromobutyl)-hydantoin-3-$N^{14}$, and this inevitably led to a dilution of the marker [6].

It was obvious that this undesirable reaction could be prevented by substituting some radical for the 3-NH hydrogen of 5-( $\delta$-bromobutyl)-hydantoin. We therefore decided to use 5-( $\delta$-bromobutyl)-3-phenylhydantoin for the condensation with potassium phthalimide-$N^{15}$, and prepared it by two methods. We first synthesized it from the previously described 5-( $\delta$-benzoylaminobutyl)-3-phenylhydantoin [7], which was easily obtained from $\epsilon$-N-benzoyllysine:

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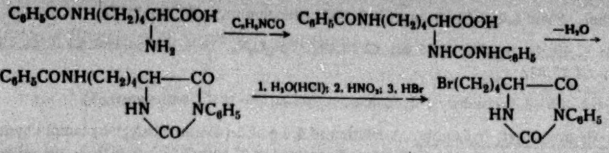
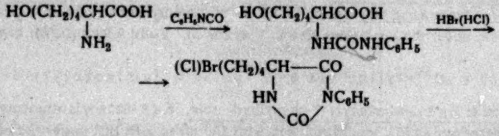
* For the previous paper in this series see [1].



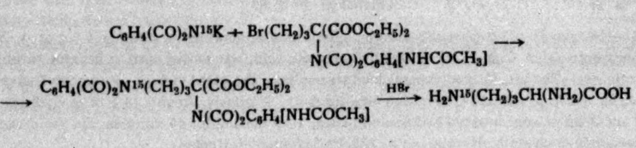
It was found that the racemic 5-(δ-benzoylaminobutyl)-3-phenylhydantoin hydrolyzed quite satisfactorily, although Karrer and Ehrenstein [8] had been unable to hydrolyze the D-isomer. But the final yield of 5-(δ-bromobutyl)-3-phenylhydantoin was low, owing to the difficulty in replacing the amino group by hydroxyl (see above).

A much better yield of 5-(δ-halogenobutyl)-3-phenylhydantoin was obtained from ε-hydroxy-α-aminocaproic acid:



The 5-(δ-bromobutyl)-3-phenylhydantoin, synthesized in this way, was condensed, under the previously described conditions [2], with potassium phthalimide-$N^{15}$ in dimethylformamide, and the resulting phthaloyl derivative was hydrolyzed with $Ba(OH)_2$ and then with HCl, to give the monohydrochloride of ε-$N^{15}$-lysine in 65% yield, based on the potassium phthalimide-$N^{15}$. Investigation of the isotopic composition of the nitrogen, in the starting material and final product, showed (see Table) that this synthesis of ε-$N^{15}$-lysine was not accompanied by any dilution of the marker.

δ-$N^{15}$-Ornithine. At first, by analogy with lysine, we used unlabelled ornithine as starting material, and converted it via α,δ-bis-(phenylureido)-valeric acid to the hydrochloride of 5-(γ-aminopropyl)-3-phenylhydantoin. But attempts to convert the latter (via the corresponding hydroxy derivative) into 5-(γ-bromopropyl)-3-phenylhydantoin were unsuccessful. δ-$N^{15}$-Ornithine was subsequently synthesized by the condensation of potassium phthalimide-$N^{15}$ with (γ-bromopropyl)-N-phthaloylaminomalonic ester and also with (γ-bromopropyl)-N-acetylaminomalonic ester. Subsequent hydrolysis and decarboxylation of the phthaloyl derivatives gave labelled ornithine in 65-70% yield, based on the potassium phthalimide-$N^{15}$. There was no dilution of the marker in this synthesis (see Table).



$$C_6H_4(CO)_2N^{15}K + Br(CH_2)_3\underset{N(CO)_2C_6H_4[NHCOCH_3]}{C}(COOC_2H_5)_2 \longrightarrow$$

$$\longrightarrow C_6H_4(CO)_2N^{15}(CH_2)_3\underset{N(CO)_2C_6H_4[NHCOCH_3]}{C}(COOC_2H_5)_2 \xrightarrow{HBr} H_2N^{15}(CH_2)_3CH(NH_2)COOH$$

## EXPERIMENTAL

### 1. Preparation of ε-$N^{15}$-Lysine Via 5-(δ-phthaloylaminobutyl)-hydantoin

a) 5-(δ-Benzoylaminobutyl)-hydantoin. A solution of 12.0 g of ε-N-benzoyllysine and 5.76 g of urea in 600 ml of water was boiled for 10-15 hours, acidified with concentrated hydrochloric acid, boiled again for 5 minutes and cooled, and the deposit formed was filtered off. Yield 9.4 g (71%); m.p. 182-183° (from alcohol) [10].

b) Hydrochloride of 5-(δ-aminobutyl)-hydantoin. A mixture of 10.0 g of 5-(δ-benzoylaminobutyl)-hydantoin and 250 ml of 20% HCl was boiled for 10 hours, cooled and filtered, the solution was extracted with ether, and the aqueous layer was evaporated to dryness under reduced pressure. The residue was dissolved in 10 ml of boiling water, and the amine hydrochloride was precipitated by addition of 30 ml of alcohol and recrystallized from 50% alcohol. Yield 4.0 g (53%); m.p. 208-209° (literature m.p. [5] 163-170°).

Found %: C 40.55; H 6.75; N 19.96; Cl 17.10. $C_7H_{13}O_2N_3 \cdot HCl$. Calculated %: C 40.48; H 6.79; N 20.24; Cl 17.07.

The picrate of 5-(δ-aminobutyl)-hydantoin melted at 180-184° (from water) [5].

c) 5-(δ-Hydroxybutyl)-hydantoin. A solution of 4.0 g of 5-(δ-aminobutyl)-hydantoin hydrochloride in 5.2 ml of N HCl was diluted with 20 ml of water, diazotized at 0° with 2.12 g of $NaNO_2$ and allowed to stand at room temperature for 4 hours. The solution was evaporated under reduced pressure to a small bulk, and the deposit was filtered off. Yield 0.76 g (23%); m.p. 152-154° [5, 6].

d) 5-(δ-Bromobutyl)-hydantoin was obtained as described previously [5]. Yield 70% ; m.p. 129-130° (from water).

e) The hydrochloride of ε-$N^{15}$-lysine was prepared by the condensation of 0.55 g of potassium phthalimide-$N^{15}$ with 0.70 g of 5-(δ-bromobutyl)-hydantoin in 3.5 ml of dimethylformamide, and subsequent hydrolysis of the phthaloyl derivative, under the conditions give in 2 d) and e). Yield 0.29 g (53%); m.p. 256-257°.

### 2. Preparation of ε-$N^{15}$-lysine via 5-(δ-phthaloylaminobutyl)-3-phenylhydantoin

a) Hydrochloride of 5-(δ-aminobutyl)-3-phenylhydantoin. 5-(δ-Benzoylaminobutyl)-3-phenylhydantoin (3.51 g), prepared as described in [7], was hydrolyzed with 100 ml of 20% HCl under the conditions described in 1 b). The deposit formed was dissolved in 2 ml of water, and the solution was cooled to 0°. A small quantity of the starting material was deposited and filtered off, and the filtrate was evaporated. The yield was 2.48 g (69%) of the amine hydrochloride, of m.p. 155-160° (purified by precipitation from alcohol with ether).

Found %: Cl 12.76. $C_{13}H_{17}O_2N_3 \cdot HCl$. Calculated %: Cl 12.54.

The picrate of 5-(δ-aminobutyl)-3-phenylhydantoin melted at 168° (from water).

Found %: C 47.70; H 4.22. $C_{19}H_{20}O_9N_6$. Calculated %: C 47.90; H 4.23.

b) 5-(δ-Bromobutyl)-3-phenylhydantoin. A solution of 1.42 g of 5-(δ-aminobutyl)-3-phenylhydantoin hydrochloride in 8 ml of 30% $CH_3COOH$ was diazotized with 0.76 g of $NaNO_2$. The solution was extracted with ethyl acetate, the extract was washed a few times with water and dried over $Na_2SO_4$, and the solvent was evaporated under reduced pressure. The resulting uncrystallized oil was boiled for 10 minutes with 6 ml of 48% hydrobromic acid, and the deposit, which formed on cooling, was filtered off and crystallized from 50% alcohol; this gave 0.15 g (10%) of 5-(δ-bromobutyl)-3-phenylhydantoin of m.p. 125-126°.

Found %: Br 26.17. $C_{13}H_{15}O_2N_2Br$. Calculated %: Br 25.63.

c) 5-(δ-Halogenobutyl)-3-phenylhydantoin. The solution, obtained by heating 4.0 g of ε-hydroxy-α-phenylureidocaproic acid* with 25 ml of 48% hydrobromic acid, was boiled until it became turbid and then for a further 10 minutes. The oil, formed, crystallized on cooling; the yield of 5-(δ-bromobutyl)-3-phenylhydantoin was 4.31 g (92%), the m.p. was 125-126° (from 50% alcohol). Similarly, from 0.53 g of ε-hydroxy-α-phenylureidocaproic acid and 3 ml of concentrated hydrochloric acid, after boiling for 40 minutes, the yield was 0.16 g (30%) of 5-(δ-chlorobutyl)-3-phenylhydantoin; m.p. 121-122° (from 50% alcohol).

Found %: C 58.51; H 5.75. $C_{13}H_{15}O_2N_2Cl$. Calculated %: C 58.54; H 5.68.

d) 5-(δ-$N^{15}$-Phthaloylaminobutyl)-3-phenylhydantoin. Potassium phthalimide-$N^{15}$ (1.11 g) was dried at 200° and 0.05 mm, and treated with 1.87 g of 5-(δ-bromobutyl)-3-phenylhydantoin and 15 ml of dimethylformamide. The mixture was heated for 1 hour at 90-95° and poured into 35 ml of water. The product was cooled for 2 hours at 0°, after which 1.64 g of the phthaloyl derivative was filtered off; evaporation of the mother liquor gave another 0.33 g. Total yield 87%; m.p. 202-203° (from chloroform).

Found %: C 66.80; H 5.02; N 11.16. $C_{21}H_{19}O_4N_3$. Calculated %: C 66.83; H 5.07; N 11.13.

e) Monohydrochloride of ε-$N^{15}$-lysine. A mixture of 1.13 g of the $N^{15}$-phthaloyl derivative (obtained in

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* This was obtained in 85% yield by the action of $C_6H_5NCO$ on ε-hydroxy-α-aminocaproic acid [5].

TABLE

Isotopic Composition of Nitrogen in the Compounds Synthesized

| Experiment No. | Title of experiment | Compound investigated | $N^{15}$ content (atoms %) | |
|---|---|---|---|---|
| | | | found | calculated |
| 1 | Preparation of ε-$N^{15}$-lysine via 5-(δ-phthaloylaminobutyl)-hydantoin. | a) Potassium phthalimide-$N^{15}$ | 21.8 | |
| | | b) ε-$N^{15}$-Lysine hydrochloride | 6.0 | (21.8 + 0.38) : 2 = 11.1 |
| 2 | Preparation of ε-$N^{15}$-lysine via 5-(δ-phthaloylaminobutyl)-3-phenylhydantoin | a) Potassium phthalimide-$N^{15}$ | 36.0 | |
| | | b) 5-(δ-Phthaloylaminobutyl)-3-phenylhydantoin. | 12.3 | (36.0 + 2 · 0.38) : 3 = 12.2 |
| | | c) ε-$N^{15}$-Lysine hydrochloride | 17.8 | (36.0 + 0.38) : 2 = 18.2 |
| 3. | Preparation of δ-$N^{15}$-ornithine via the diethyl ester of α,ω-diphthaloylaminopropylmalonic acid | a) Potassium phthalimide-$N^{15}$ | 36.0 | |
| | | b) δ-$N^{15}$-Ornithine hydrochloride | 18.2 | (36.0 + 0.38) : 2 = 18.2 |
| 4 | Preparation of δ-$N^{15}$-ornithine via the diethyl ester of α-acetylamino-ω-phthaloylaminopropylmalonic acid | a) Potassium phthalimide-$N^{15}$ | 36.0 | |
| | | b) δ-$N^{15}$-Ornithine hydrochloride | 17.9 | (36.0 + 0.38) : 2 = 18.2 |

experiment 2 d), 3.5 g of $Ba(OH)_2 \cdot 8\,H_2O$ and 15 ml of water was heated with shaking, in a sealed tube, at 160-165°, for 1 hour. The mixture was cooled, barium carbonate was separated, 1 g of ammonium carbonate was added, the liquid was filtered again, the filtrate was extracted with chloroform to remove aniline, and the aqueous layer was then evaporated almost to dryness (finally under reduced pressure). The residue was dissolved in 7 ml of water, acidified with concentrated hydrochloric acid, treated with a further 15 ml of 5 N hydrochloric acid and boiled for 1 hour. Phthalic acid was filtered off, the filtrate was evaporated to dryness under reduced pressure, and the residue was dissolved in 2-3 ml of water and again evaporated. The residue was dissolved in 15 ml of boiling absolute alcohol, lysine monohydrochloride was precipitated by adding a hot mixture of 2 ml of pyridine and 3 ml of alcohol, half the alcohol was distilled off, the liquid was cooled, and the deposit was filtered off, washed with alcohol and ether and dried. Yield 0.43 g (78%); m.p. 254-255°.

### 3. Preparation of δ-$N^{15}$-Ornithine Via the Diethyl Ester of α,ω-Diphthaloylaminopropylmalonic Acid.

Dimethylformamide (10 ml) and 40 ml of trimethylene bromide were added to 16.35 g of the dry sodium derivative of the diethyl ester of phthaloylaminomalonic acid [11]. The mixture was heated for 1.5 to 2 hours, at 85-95°, until quite colorless, NaBr was separated, the filtrate was evaporated, the residue was stirred with 25-30 ml of hot chloroform, and the whole was cooled for 2 hours at 0° and filtered. Evaporation of the chloroform gave 20.0 g (94%) of the diethyl ester of (γ-bromopropyl)-N-phthaloylaminomalonic acid in the form of an uncrystallized oil (cp. [12]). A solution of 15.7 g of this ester in 15 ml of dimethylformamide was treated with 5.55 g of potassium phthalimide-$N^{15}$, and the mixture was heated for 1 hour at 90-95°. The KBr was filtered off quickly and washed with hot $CHCl_3$, the filtrate was allowed to stand at 0° for 24 hours, and the deposited diphthaloyl derivative was filtered off under suction and washed with ether. Yield 11.3 g (76%); m.p. 130-133° (from alcohol).

Found %: C 63.50; H 4.93; N 5.75. $C_{26}H_{24}O_8N_2$. Calculated %: C 63.41; H 4.91; N 5.69.

The hydrolysis of the diphthaloyl derivative and the isolation of the monohydrochloride of δ-$N^{15}$-ornithine were carried out normally [2]. Yield 3.51 g (70 %); m.p. 222-224°.

### 4. Preparation of δ-$N^{15}$-Ornithine Via the Diethyl Ester of α-Acetylamino-ω-phthaloylaminopropylmalonic Acid

A mixture of 0.92 g of potassium phthalimide-$N^{15}$, 1.70 g of (γ-bromopropyl)-N-acetylaminomalonic ester [13] and 5 ml of dimethylformamide was heated for 1 hour at 85-95°. The KBr was filtered off, the filtrate was evaporated under reduced pressure, the residue was stirred with 15 ml of boiling chloroform, and the solution was filtered and evaporated. The phthaloyl derivative obtained (2.17 g; 85%)* was hydrolyzed with a mixture of 5 ml of $CH_3COOH$, 5 ml of water and 5 ml of HBr for 22 hours [2]. The yield of the monohydrochloride of δ-$N^{15}$-ornithine was 0.55 g (65%); m.p. 222-224°.

### 5. Attempt to Prepare δ-$N^{15}$-Ornithine Via 5-(γ-phthaloylaminopropyl)-3-phenylhydantoin

A solution of 3.37 g of the monohydrochloride of ornithine in 20 ml of N NaOH was treated with 4 ml of phenylisocyanate, and the mixture was stirred vigorously (it became hot) until the smell of the isocyanate had disappeared. Traces of diphenylurea were filtered off, the solution was acidified with 1 : 1 HCl, and the deposit was filtered off, washed with water and dried. The yield of α,δ-di-(phenylureido)-valeric acid was 6.77 g (91.4%); m.p. 167° (decomp.) [9].

A mixture of 10.85 g of this product and 270 ml of 20% HCl was boiled for 20 hours, the solution was evaporated under reduced pressure, and the residue was diluted with 10 ml of water. There was a deposit of 1.43 g (14%) of 5-(γ-phenylureidopropyl)-3-phenylhydantoin, of m.p. 189-190° [9]. The filtrate was evaporated to dryness, and the residue was dissolved, by heating, in 35-40 ml of absolute alcohol. 5-(γ-Aminopropyl)-3-phenylhydantoin hydrochloride was deposited on cooling. Yield 4.52 g (66%); m.p. 217-218° (from alcohol).

Found %: C 53.48; H 6.06; N 15.45. $C_{12}H_{15}O_2N_3 \cdot HCl$. Calculated %: C 53.43; H 5.98; N 15.58.

An attempt to convert 5-(γ-aminopropyl)-3-phenylhydantoin into the corresponding bromo derivative (using the conditions of experiment 2 b) did not lead to the isolation of the desired substance.

## SUMMARY

The syntheses of two ω-$N^{15}$-amino acids – ε-$N^{15}$-lysine and δ-$N^{15}$-ornithine – are described.

## LITERATURE CITED

[1] M. M. Shemiakin, V. I. Maimind and B. K. Vaichunaite, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1957,** 1260.

[2] V. I. Maimind, K. M. Ermolaev and M. M. Shemiakin, J. Gen. Chem., 26, 2313 (1956).**

[3] V. I. Maimind, B. V. Tokarev, E. Gomes, R. G. Vdovina, K. M. Ermolaev and M. M. Shemiakin, J. Gen. Chem. 26, 1962 (1956).**

[4] R. M. Fink, T. Euns, C. P. Kimball, H. E. Silberstein, W. F. Bale, S. C. Madden, and G. H. Whipple, J. Exp. Med., 80, 455 (1944).

[5] R. Gaudry, Canad. J. Res., 26B, 387 (1948).

[6] A. O. Rogers, R. D. Emmick, L. W. Pyran, L. B. Phillips, A. A. Levine and N. D. Scott, J. Am. Chem. Soc., 71, 1837 (1949).

[7] J. Braun, Ber., 42, 845 (1909).

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* After recrystallization from 50% alcohol this melted at 111-112°. Found %: N 7.23; $OC_2H_5$ 22.51. $C_{20}H_{24}O_7N_2$. Calculated %: N 6.93; $OC_2H_5$ 22.29.

**Original Russian pagination. See C.B. translation.

[8] P. Karrer, and M. Ehrenstein, Helv. Chim. Acta, 9, 328 (1926).

[9] H. D. Dakin, J. Biol. Ch., 146, 237 (1942).

[10] V. I. Maimind, B. V. Tokarev and M. M. Shemiakin, Proc. Acad. Sci. USSR, 92, 81 (1953).

[11] Synth. Org. Prep. II, 340 (1949).*

[12] S. P. L. Sörensen, Z. physiol. Ch., 44, 448 (1905).

[13] M. Rothstein and C. J. Claus, J. Am. Chem. Soc., 75, 2981 (1953).

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*In Russian.

# MOLECULAR STRUCTURE OF UNSATURATED KETONES – BIMOLECULAR CYCLOHEXANONE CONDENSATION PRODUCTS

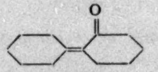
Ts. N. Roginskaia, S. V. Svetozarskii, A. I. Finkel'shtein,
and E. N. Zil'berman

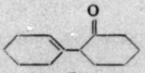
Wallach [1] prepared the first liquid bimolecular cyclohexanone condensation product (unsaturated ketone with empirical formula $C_{12}H_{18}O$ (I) ) through the action of sodium ethoxide on cyclohexanone over a period of many days. Later, after passing gaseous HCl through pure cyclohexanone, Wallach [2] isolated a compound $C_{12}H_{19}OCl$ and again obtained (I) by splitting out HCl. This compound has also been synthesized by treating cyclohexanone with a methanol solution of sulfuric acid [3], calcium hydride [4, 5], calcium carbide [4], zinc chloride [6], aluminum oxide [7], sodium amide [8], et al.

Depending on reaction conditions, compound (I) can react as an $\alpha,\beta$- or $\beta,\gamma$-unsaturated ketone, or as a mixture of both. Compound (I) behaves like $\alpha,\beta$-unsaturated ketones on hydration in the presence of solid catalysts [9], in interaction with benzaldehyde, hydrogen chloride, cyclohexanone [6], condensation with ethyl sodiumcyanoacetate [10], and in Kishner reaction [11]. The absence of any substantial optical exaltation in the molar refraction [10, 12] is considered as evidence for the endocyclic nature of the double bond in compound (I).

Compound (I) acts as a $\beta,\gamma$-unsaturated ketone in reaction with nascent hydrogen [9, 13], oxidation with ozone [10] and potassium permanganate [12], and methylation with methyl iodide [10]. When compound (I) is oxidized with alkaline hydrogen peroxide, both $\alpha,\beta$- and $\beta,\gamma$-unsaturated ketone derivatives are obtained [12].

On the basis of chemical properties, ketone (I) was assigned structure (A) [6, 9-11] or (B) [9, 10, 12-14], or considered a mixture of isomers (A) and (B) [15, 16].


(A)


(B)

The supporters of structure (B) [10, 14], rely not only on chemical reactions of (I) but refer also to the Dieckmann-Kon rule, according to which a semicyclic (exo) double bond in a cyclohexane ring is less stable than an endocyclic double bond.

The problem of ketone (I) structure was complicated by the fact that in 1942 Reese [12] discovered a new unsaturated ketone, $C_{12}H_{18}O$ (II), which, without any doubt, had a double bond in $\alpha,\beta$-position (judging by its behavior in a series of reactions). Unlike compound (I) it was solid (m.p. 57°). Compound (II) was comparatively unstable and changed into liquid ketone (I) when heated.

The spectra of ketones (I) and (II) have not been up till now systematically investigated. Only the ultraviolet spectrum of compound (I) was known, and it indicated [16] the presence of an $\alpha,\beta$-conjugated double bond in this ketone ($\lambda_{max}$ = 255 m$\mu$, $\epsilon_{max}$ = 6300).

Vibrational spectra (infrared and Raman) of ketone (I) had not been determined. Spectroscopic investigation of ketone (II) had not been conducted, and only very recently (after completion of this work) has a paper appeared [17] in which some spectral absorption data are listed, but without any kind of discussion.

We carried out an investigation of the optical properties of ketones (I) and (II) in order to obtain some data on the molecular structure of these compounds. The Raman spectra we obtained for ketones (I) and (II) are shown in the Table, the infrared absorption spectra in Fig. 1 and 2, the ultraviolet in Fig. 3 (methanol solutions) and 4 (diethyl ether solutions).

Raman Spectra of Ketone (I) and (II)

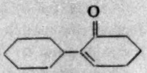
| Ketone (I) | Ketone (II) ($CCl_4$ solution) |
|---|---|
| | 257 (1) |
| | 276 (1) |
| 695 (0) | 671 (0) |
| 839 (1) | 845 (1) |
| 956 ($^1/_2$) | |
| 1040 (0) | 1031 (2) |
| | 1056 (2) |
| 1125 (1) | |
| | 1227 (?) |
| 1270 (2) | 1249 (2) |
| | 1323 (3) |
| | 1346 (0) |
| 1417 (10 b) | 1442 (5) |
| 1592 ($^1/_2$) | |
| | 1612 } (10 b) |
| 1628 (2) | 1628 |
| 1690 (3) | 1668 (1) |
| 2847 (5) | 2847 (3) |
| 2953 (5) | 2930 (2) |

Electronic as well as vibrational spectra of ketones (I) and (II) show that both of these compounds are $\alpha,\beta$-unsaturated ketones. This is proven by the presence of 1628 and 1690 $cm^{-1}$ frequencies in the Raman spectrum of ketone (I). Similarly, in the Raman spectrum of ketone (II) 1628 and 1679 $cm^{-1}$ frequencies are observed, indicating that this compound is also an $\alpha,\beta$-unsaturated ketone. No lines were detected in the 1710 and 1650-1660 $cm^{-1}$ frequency region; these lines are characteristic of ketones with unconjugated double bonds. There was no indication of enolization. Weak bands at 1591 $cm^{-1}$ (ketone (I)) and 1612 $cm^{-1}$ (ketone (II)) were evidently connected with Fermi resonance.

In the infrared absorption region we observed the characteristic frequencies of conjugated carbonyl compounds. They were 1700 and 1626 $cm^{-1}$ for ketone (I), 1626 and 1681 $cm^{-1}$ for ketone (II). A slight increase in the infrared C=O frequency of ketone (I) was due to superposition of air absorption on the band.

In the 2-4 $\mu$ region we detected absorption bands which could only be due to C–H groups (one has to consider the accuracy of frequency determination with a NaCl prism). We were unable to detect any supplementary absorption bands which could be attributed to O–H groups; this indicated the absence of any detectable signs of keto – enol tautomerism.

The ultraviolet absorption spectra of ketone (I) and (II) differ only in the size of extinction coefficients ($\epsilon_{max}$ = 6,200 moles/liter · cm for ketone (I) and 14,200 moles/liter · cm for ketone (II)). Both ketones have an absorption maximum at the same wavelength ($\lambda_{max}$ = 254 m$\mu$); according to Woodward's rule [18], this wavelength corresponds to trisubstituted conjugated unsaturated ketones. In this case it would correspond to formula (A) (with a cis-configuration of the double bond). Hence, it follows that it is impossible to assign formula (C) (with a trans-configuration of bonds) to the substances investigated.



(C)

Compound (C) should absorb at $\lambda_{max}$ = 239 ± 5 m$\mu$; this, in fact, was not observed [11]. This conclusion is supported also by chemical data.

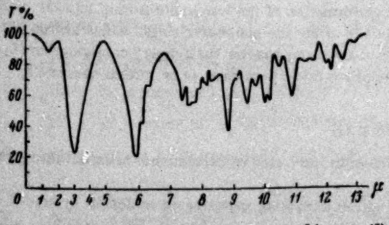


Fig. 1. Infrared absorption spectrum of ketone (I).

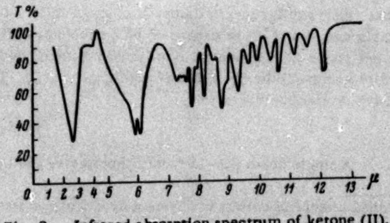


Fig. 2. Infrared absorption spectrum of ketone (II).

The sharp decrease of absorption coefficient in the ultraviolet spectrum of ketone (I) could not be explained by the presence of ketone (B), since the corresponding frequencies in the vibrational spectrum were not observed. Thus, both ketone (I) and (II) are $\alpha,\beta$-unsaturated ketones. The behavior of compound (I) as $\beta,\gamma$-unsaturated in a series of reactions can be explained as being due to a transition of compound (I) into a substance of structure (B) during the course of reaction.

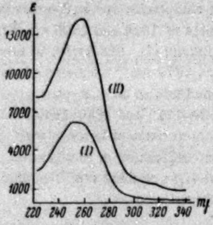


Fig. 3. Ultraviolet absorption spectra of ketones (I) and (II) in methyl alcohol.

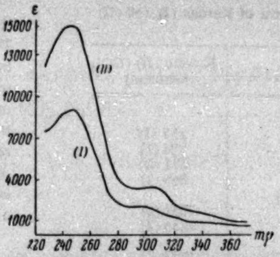


Fig. 4. Ultraviolet absorption spectra of ketones (I) and (II) in diethyl ether.

The most probable cause of the existence of two 2-cyclohexylidenecyclohexanones with different physical and chemical properties could be the difference in the forms of six-membered rings of these compounds. As is well known, cyclohexane rings can exist in a boat or chair configuration; actually, only the chair form is found to be energetically favorable. Similar configurations can also be observed in 2-cyclohexylidenecylohexanone, while due to a stereochemical deformation of six-membered rings, the boat form (usually less stable) may in this case become more stable than the corresponding configuration of cyclohexane [19]. In Fig. 5 we have shown the two possible stereochemical configurations of 2-cyclohexylidenecyclohexanone. One should emphasize the difference in the ring structure itself. Both ketones are composed of identical rings, but one ring of each has a single $sp^2$ hybrid, while the other, two. If the cyclohexylidene ring differs only very slightly from a cyclohexane ring (an increase in angle $\alpha$ is compensated by a decrease in bond lengths $r_1$ and $r_2$),* then the other ring (which contains two $sp^2$ hybrids) should differ very sharply from it. Three bonds of the second ring lie in the same plane; therefore, interconversion of stereochemical configurations is made easier [19], and both configurations (D) and (E) (half-chair and half-boat) become equivalent and stable, just as in the case of cyclohexene. Consequently, the existence of two (liquid (I) and solid (II)) isomeric forms of 2-cyclohexylidenecyclohexanone, their similar spectral properties, and a relatively easy transformation of the less stable isomer into the more stable one, could all be explained by a structural difference in one of the six-membered rings. Since ketone (II) is less stable (it is converted into liquid ketone (I) on heating), it evidently has the "half-boat" configuration (E), while ketone (I), the "half-chair" configuration (D). The assumptions made here have to be further checked by X-ray or electron diffraction.

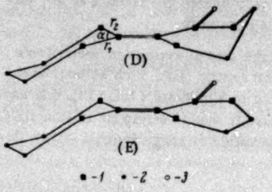


Fig. 5. Stereoisomers of 2-cyclohexylidenecyclohexanone.
1) Carbon atoms located in the main plain; 2) carbon atoms out of the main plain; 3) oxygen atoms. Explanation is in the text.

## EXPERIMENTAL

A single beam IKS-11 spectrophotometer and a rock salt prism were used to determined infrared absorption spectra. Raman spectra were determined on a triprismatic glass spectrograph ISP-51. For the input radiation we used the 4358 A mercury line emitted by a light filter made with a saturated aqueous $NaNO_2$ solution or a standard glass light filter Hg 456. For the ultraviolet absorption spectra we used a quartz spectrophotometer SF-4.

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* Bond lengths of carbon in different hybridization states ($sp^3$, $sp^2$, and sp) were investigated in detail by one of the authors somewhere else.

Ketone (I) was obtained by condensing cyclohexanone in the presence of sulfuric acid [20]: b.p. 142° (13 mm), $n^{20}D$ 1.5074, $d^{20}_4$ 1.002. Ketone (II) was synthesized according to Reese [12] and had a m.p. 57°.

In concluding, we would like to express our gratitude to G. A. Razuvaev for his interest in this work and valuable advice.

## SUMMARY

1. We have studied the ultraviolet and infrared absorption spectra, and also the Raman spectra in order to elucidate the molecular structure of the two isomeric unsaturated ketones – bimolecular products of cyclohexanone condensation.

2. We have shown that both compounds were just two different configurations of 2-cyclohexylidenecyclohexanone.

3. A hypothesis is proposed that the isomers differ from each other only in the stereochemical structure of the ring containing the carbonyl group.

## LITERATURE CITED

[1] O. Wallach, Ber., 29, 2965 (1896).

[2] O. Wallach, Ber., 40, 70 (1907).

[3] C. Mannich, Ber., 40, 153 (1907).

[4] F. Taboury and M. Godchot, C. r., 169, 62 (1918).

[5] G. Vavon, Anziani and Herynk, Bull. Soc. Chim., (4), 39, 1138 (1926).

[6] K. Kunze, Ber., 59, 2085 (1926).

[7] A. Petrov, Bull. Soc. Chim., (4), 43, 1272 (1928).

[8] A. Haller and E. Bauer, C. r., 162, 551 (1911).

[9] W. Hückel, Lieb. Ann., 487, 99 (1930).

[10] G. A. R. Kon and J. H. Nutland, J. Chem. Soc., 1926, 3101.

[11] N. D. Zelinskii, N. I. Shuikin, L. M. Fateev, J. Gen. Chem.,2, 671 (1932).

[12] J. Reese, Ber., 75, 384 (1942).

[13] O. Wallach, Lieb. Ann., 381, 95 (1911).

[14] H. C. Brown, J. H. Brewster and H. Shechter, J. Am. Chem. Soc., 76, 467 (1954).

[15] J. Plesek, Chem. Listy, 50, 252 (1956).

[16] H. S. French and L. Wiley, J. Am. Chem. Soc., 71, 3702 (1949).

[17] H. O. House and R. L. Wasson, J. Am. Chem. Soc., 78, 4394 (1956).

[18] R. B. Woodward, J. Am. Chem. Soc., 63, 1123 (1941).

[19] I. N. Nazarov, L. D. Bergel'son, Prog. Chem. 26, 3 (1957).

[20] H. Gault, L. Daltrott and I. Eck-Fridon, Bull. Soc. Chim., 12, 952 (1945).

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# REACTIONS OF ACYL PEROXIDES WITH METALS

G. A. Razuvaev and V. N. Lamiaeva

We have noted in our previous work [1] that the decomposition of acyl peroxides with metallic mercury was observed at comparatively low temperatures. At room temperature the acyloxy radicals formed the corresponding mercury salts. When the temperature was raised, a partial decarboxylation of acyloxy radicals and a formation of organomercury compounds was observed.

As is well known, the fixation of free acetyloxy radicals on metals was utilized by Waters [2] in his investigation of benzene diazoacetate decomposition with Zn, Fe, Cu, Hg and other metals in nonpolar solvents; in all the cases the corresponding metal acetates were produced. G. A. Razuvaev and M. M. Koton [3, 4] have used metals to study the catalytic decomposition of organometallicmercury, lead, and tin compounds. It was shown, that addition of metals lowered considerably the temperature barrier in these reactions. The type of metal added influenced the reactivity of free radicals. The catalytic decomposition of acyl peroxides in the presence of metals has been studied very little. We can mention the work of F. I. Berezovskaia and O. N. Semikhatova [5] on the catalytic decomposition of benzoyl and acetylbenzoyl peroxides in the presence of Pt and $MnO_2$. The authors have shown that the decomposition of benzoyl peroxide in ether was catalyzed by platinum only if water was present; evolution of oxygen was observed during this reaction. The reaction products were not isolated, and the reaction mechanism remained uncertain.

G. A. Razuvaev and co-workershave studied [6] the reactions of benzoyl peroxide with lead dichloride, antimony trichloride, and metallic lead. It was established that $SnCl_2$ and metallic tin were very active acceptors of benzoyloxy radicals. In dichloroethane and acetic anhydride at room temperature and while in benzene at its boiling point,a quantitative yield of tin benzoates $(C_6H_5COO)_4Sn$ and $(C_6H_5COO)_2SnCl_2$ was obtained. No decarboxylation or solvent interaction was observed with benzoyloxy radicals.

We considered it worthwhile to make a more detailed study of the effect of various metals on the decomposition of symmetrical and unsymmetrical acyl peroxides in solutions. We decided to put a special emphasis on reactions in alcohols (active hydrogen donors). With this in mind, we studied decomposition of benzoyl peroxide and acetylbenzoyl peroxide in methyl, ethyl, and isopropyl alcohols, chloroform, $CCl_4$, and $C_6H_6$ in the presence of Na, Zn, Cu, Fe, Ni, Ag, and Pt at room temperature; several reactions were also carried out with phenacyl, phenacylbenzoyl, and p-nitrobenzoylbenzoyl peroxides. Experiments carried out with benzoyl peroxide showed that a quantitative yield of benzoates was obtained with Na (2% amalgam) and Zn in benzene and alcohol solutions. It is interesting to note that no mercury salts were formed when Na amalgam was used. With Ni and Fe in alcohol, only a part of the benzoyloxy radicals was converted into anions. Beside salts the reaction products contained free benzoic acid and aldehydes; formation of these could be explained by dehydration of alcohol with benzoyloxy free radicals. The presence of the latter was confirmed by a rapid discoloration of diphenylpicrylhydrazyl which is used as a free radical indicator.

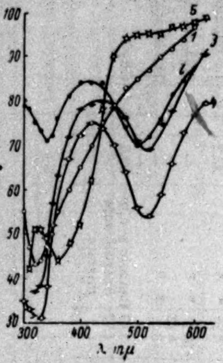
The course of the above described reactions could be described in the following manner. In one case the peroxide accepted 2 electrons from the metal and formed a benzoate anion.

$$(C_6H_5CO_2)_2 + Zn \rightarrow 2C_6H_5COO^- + Zn^{2+}$$

A similar reaction took place with sodium. In another case there was a transfer of one electron with the formation of a benzoate anion and a benzoyloxy radical.

$$(C_6H_5CO_2)_2 + Met \rightarrow C_6H_5COO^- + Met^+ + C_6H_5COO\cdot$$
$$Met{=}Ni,\ Fe,\ Cu.$$

The last one reacted with the solvent (alcohol). A univalent metallic cation may be raised to a higher oxidation state. In connection with this, it was interesting to see which group in an unsymmetrical peroxide would accept an electron and change into anion. For this purpose we investigated the acetylbenzoyl peroxide in more detail and conducted several experiments on p-nitrobenzoylbenzoyl, phenacyl, and phenacylbenzoyl peroxides.



Diphenylpicrylhydrazine (DPhPH-ine) and diphenylpicrylhydrazyl (DPhPH-yl) absorption spectra in the presence of acetylbenzoyl peroxide in $CH_3OH$.

1) DPhPH-ine; 2) DPhPH-yl;
3) reaction mixture after 10 minutes;
4) reaction mixture after 30 minutes;
5) reaction mixture after 24 hours.

Similar results were obtained with acetylbenzoyl peroxide; with Na, Hg, and Zn acetates and benzoates formed simultaneously (in alcohols as well as in benzene), while with Ni, Cu, and Ag, formation of metallic acetates and free benzoic acid was observed. With these metals the presence of free radicals was confirmed by testing with diphenylpicrylhydrazyl. When we added diphenylpicrylhydrazine, in place of diphenylpicrylhydrazyl, to an alcoholic solution of acetylbenzoyl peroxide, the initial yellow color of solution changed very rapdily to violet (due to diphenylpicrylhydrazyl formation) and then slowly decolorized; this was another indication of free radicals. Conversion of diphenylpicrylhydrazine into diphenylpicrylhydrazyl was also confirmed through spectral analysis of the reaction mixture (see the Figure). After the reaction of platinum with acetylbenzoyl peroxide in ethyl alcohol we isolated acetic acid, benzoic acid, and formaldehyde from among the reaction products. Decomposition of acetylbenzoyl peroxide with copper in chloroform gave mainly Cu acetate and benzoate (75 and 63% respectively, see the Table, exp. 15). Besides these, benzoic acid is also formed (22%). One should note, that in this case we observed noticeable chlorination of metals, initiated by the peroxide (see the Table, exp. 14, 15, 16); previous indications of this are found in the literature [7].

Reaction of p-nitrobenzoylbenzoyl peroxide with Cu in $CH_3OH$ was accompanied by the formation of corresponding salts as well as free acids.

Under similar conditions the reaction with phenacyl and phenacylbenzoyl peroxides was more complex. In the case of phenacylbenzoyl peroxide, evolution of $CO_2$ (at the expense of phenacyloxy radical) and formation of copper benzoate were observed. We found formaldehyde, free phenylacetic and benzoic acids, and dibenzyl in solution. The formation of the last one could be explained by the relative instability of $C_6H_5CH_2COO$-radical which often decomposes with the evolution of $CO_2$. The more stable benzyl radical that is formed dimerizes, then into dibenzyl. The rest of the $C_6H_5CH_2COO$-radicals dehydrate the alcohol, forming phenylacetic acid and formaldehyde.

$$C_6H_5CH_2COO\cdot \left\langle \begin{array}{l} \xrightarrow{CH_3OH} C_6H_5CH_2COOH + CH_2O \\ \xrightarrow{-CO_2} C_6H_5CH_2\cdot \rightarrow (C_6H_5CH_2)_2 \end{array} \right.$$

Thus, the small reactivity of benzyl radical (frequently observed before [8]) was confirmed in this case.

On the basis of results obtained, we can divide the peroxide reactions with metals into three groups. 1) Reactions with a transfer of two electrons and formation of corresponding metal salts. The solvent does not participate in these reactions (Met. = Na, Zn, Hg). 2) Reactions with one electron transfer. $RCOO^-$ anion and RCOO-radical, which interacts with the solvent, are formed (Cu, Ni, Fe, Ag). 3) Oxidation – reduction reactions of peroxides with solvent catalyzed by a metal which does not form a salt itself (Pt). These reaction groups represent limiting cases. Depending on the nature of the metal, peroxide, and solvent, two types of reactions can take place simultaneously.

The effect of metal on the formation of free radicals or the fixation of both acyloxy groups as salts shows no simple connection with the activity or overvoltage series of these metals.

Reactions of Acyl Peroxides with Metals

| No. of expt. | Used in reaction | | | | | Reaction time (in hrs) | Substances isolated | | | | | | Remarks (substances isolated beside salts and acids) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | peroxide | | solvent | | metal | | salts | yield | | free acids | yield | | |
| | name | quantity in mmole | name | quantity in ml | | | | in % | in mmole | | in % | in mmole | |
| 1 | Benzoyl | 8.26 | $C_6H_6$ | 25 | Na (Hg) | 2—3 | Benzoate | 98.5 | 16.28 | — | — | — | — |
| 2 | Ditto | 4.13 | $C_6H_6$ | 25 | Zn | 50 | Ditto | 100 | 8.26 | — | — | — | — |
| 3 | „ „ | 4.13 | $CH_3OH$ | 25 | Fe | 50 | „ „ | 25 | 2.06 | Benzoic | 50 | 4.12 | 90% of peroxide reacted |
| 4 | „ „ | 8.26 | iso -$C_3H_7OH$ | 20 | Zn | 200 | „ „ | 97 | 16.0 | | — | — | |
| 5 | „ „ | 4.13 | $C_2H_5OH$ | 20 | Ni | 2 | „ „ | 30 | 2.48 | Benzoic | 70 | 5.75 | $CH_3CHO$ |
| 6 | Acetylbenzoyl | 11.1 | $C_6H_6$ | 25 | Na (Hg) | 2—3 | „ „ | 71.8 | 7.96 | — | — | — | — |
| | | | | | | | Acetate | 69.3 | 7.68 | — | — | — | — |
| 7 | Ditto | 11.1 | $CH_3OH$ | 20 | Zn | 4—5 | Benzoate | 100 | 11.1 | — | — | — | — |
| | | | | | | | Acetate | 100 | 11.1 | — | | | — |
| 8 | „ „ | 11.1 | $CH_3OH$ | 20 | Ni | 20 | Benzoate | 18.2 | 2.0 | Benzoic | 74.0 | 8.2 | $CH_2O$ |
| | | | | | | | Acetate | 45.0 | 5.0 | Acetic | 35.1 | 3.9 | 3.5 mmoles of acetic ester |
| 9 | „ „ | 11.1 | $CH_3OH$ | 20 | Pt | 20 | — | — | — | Benzoic | 100 | 11.1 | 2 mmoles of $CH_2O$ |
| | | | | | | | | | | Acetic | 96.0 | 10.7 | |
| 10 | „ „ | 5.5 | $CH_3OH$ | 25 | Hg | 8—10 | Benzoate | 82.0 | 4.5 | Benzoic | Traces | | Traces of $C_6H_5COOCH_3$ |
| | | | | | | | Acetate | 90 | — | | | | |
| 11 | „ „ | 3.57 | $C_2H_5OH$ | 10 | Ni | 1—2 | Ditto | 76.0 | 2.7 | Ditto | 70.0 | 2.5 | |
| 12 | „ „ | 2.7 | $C_2H_5OH$ | 15 | Ag | > 200 | „ „ | 29.6 | 0.8 | „ „ | 88.0 | 2.38 | $CH_3CHO$ |
| 13 | „ „ | 5.5 | $C_2H_5OH$ | 20 | Cu | 8 | „ „ | 88.0 | 4.85 | „ „ | 97.0 | 5.33 | $CH_3CHO$ |
| 14 | „ „ | 11.1 | $CHCl_3$ | 20 | Ni | 2 | Benzoate | 33.3 | 3.7 | „ „ | 55.5 | 6.15 | 3.38 mmoles of $Cl^-$ ($NiCl_2$) |
| | | | | | | | Acetate | 95.5 | 10.6 | | | | |
| 15 | „ „ | 11.1 | $CHCl_3$ | 20 | Cu | 2—3 | Acetate | 74.7 | 8.28 | „ „ | 22.2 | 2.46 | 7.6 mmoles of $Cl^-$ |
| | | | | | | | Benzoate | 63.0 | 7.0 | | | | |
| 16 | „ „ | 11.1 | $CCl_4$ | 20 | Ni | 2 | Benzoate | 92.6 | 10.2 | „ „ | — | — | 2.25 mmoles of $Cl^-$ |
| | | | | | | | Acetate | 61.5 | 6.83 | | — | — | |
| 17 | „ „ | 11.1 | $CCl_4$ | 20 | Cu | 2—3 | Acetate | 77.7 | 8.6 | „ „ | — | — | Traces of $Cl^-$ |
| | | | | | | | Benzoate | 89.0 | 9.9 | | — | — | |
| 18 | Benzoyl-p-nitrobenzoyl | 3.46 | $CH_3OH$ | 20 | Cu | 2 | Benzoate | 71.5 | 2.47 | Benzoic p-nitrobenzoic acid mixture | 59.5 | — | $CH_2O$ |
| | | | | | | | p-Nitrobenzoate | 57.0 | 1.97 | | | | |

(Continued)

| No. of expt. | Used in reaction |  |  |  |  |  | Substances isolated |  |  |  |  |  | Remarks (substances isolated beside salts and acids) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  | peroxide |  | solvent |  | metal | Reaction time (in hrs) | salts | yield |  | free acids | yield |  |  |
|  | name | quantity in mmole | name | quantity in ml |  |  |  | in % | in mmole |  | in % | in mmole |  |
| 19 | Phenacyl | 4.15 | $CH_3OH$ | 20 | Cu | 0.5—0.7 | Phenylacetate | 70.7 | 2.94 | Phenylacetic | 49.7 | 2.06 | $CH_2O$, 1.11 mmoles of $CO_2$, 0.66 mmoles of dibenzyl |
| 20 | Phenacylbenzoyl | 5.1 | $CH_3OH$ | 20 | Cu | 2 | Benzoate | 30.4 | 1.55 | Benzoic | 66.0 | 3.37 | 1.52 mmoles of $CO_2$, 0.53 mmoles of $CH_2O$ |
|  |  |  |  |  |  |  |  |  |  | Phenylacetic | 28.8 | 1.47 | 0.88 mmoles of dibenzyl |

On the basis of experiments with mixed peroxides we can make a comparison of $CH_3COO$-, $C_6H_5COO$-, $C_6H_5CH_2COO$-, p-$O_2NC_6H_4CO$-groups in their ability to form free radicals or anions. It is evident from experiments 11, 12, 13 that $CH_3COO$ group forms an anion comparatively easier than a $C_6H_5COO$ group. If one of the hydrogensin $CH_3COO$ is replaced with a phenyl group, just the reverse takes place. Thus, in the reaction of phenacylbenzoyl peroxide the $C_6H_5CH_2COO$ group did not accept and electron from copper, and no copper phenylacetate was detected among reaction products (see the Table, exps. 11, 13, 14, 15). In carbon tetrachloride the formation of free acids is not possible. $C_6H_5COO$-radicals fully interact with the metal and initiate its chlorination (see the Table, exp. 17, 16).

## EXPERIMENTAL

Starting Materials. Acetylbenzoyl peroxide was prepared from benzaldehyde and acetic anhydride using a method proposed by Nef [9]; phenacyl peroxide was made from phenacyl chloride and $H_2O_2$ using a method of Bartlett and Leffler [10]; phenacylbenzoyl peroxide was obtained from sodium perbenzoate and phenacyl chloride using a method of Wieland and Ploetz [11]; p-nitrobenzoyl chloride and sodium perbenzoate gave p-nitrobenzoylbenzoyl peroxide. Benzoyl peroxide was purified by recrystallization from a methanol — chloroform solution. Activity of peroxides was determined by iodometric titration and was found to be 95.5-98%. The metals used in these experiments were: Pt and Ag (freshly precipitated out of their salts with formaldehyde), freshly prepared Raney Ni, Fe ("kal'baum" reduced), Cu freshly plated-out from copper sulfate, zinc dust, 2% sodium amalgam. The solvents used were purified in the usual way. Water was completely removed from alcohols.

Reactions of benzoyl, acetylbenzoyl, and p-nitrobenzoylbenzoyl peroxides with metals in solution. A weighed out sample of peroxide was dissolved in the solvent, 1-2 g of metal was placed in solution, and the reaction mixture agitated on a shaker at room temperature until all peroxide disappeared. The reaction mixture was filtered remove excess metal and insoluble salts, and the filtrate distilled on a water bath. The distillate contained the aldehyde or ketone and free acids. Free acids were extracted with ether from the residue, then the salts were decomposed with inorganic acids ($H_2SO_4$, HCl) and the acids formed were extracted with ether. Quantitative acid determination was done acidimetrically. Ni content in salts was determined in the form of dimethylglyoxime derivative; iodometrical analysis gave the contents of copper and iron.

Identification of organic reaction products was done in the usual manner: formaldehyde and acetaldehyde as dimedone derivatives, acetone as 2,4-dinitrophenylhydrazone, benzoic and p-nitrobenzoic acids through the melting point of a mixed sample, acetic acid through formation of cacodyl oxide. The results of these tests are shown in the Table.

Reaction of phenacyl peroxide with freshly precipitated copper in methyl alcohol.[*] We agitated 1.12 g (4.15 mmoles) of phenacyl peroxide (95.5% activity) with 1 g of freshly precipitated copper in 20 ml of absolute methanol for 30-40 minutes at room temperature. During the reaction 25.0 ml (1.11 mmoles) of $CO_2$ was evolved; it was determined as $BaCO_3$. The reaction mixture was analyzed as described above. We isolated 0.28 g (2.06 mmoles) of free phenylacetic acid, m.p. 75° (a sample mixed with known pure substance gave no melting point depression); 0.12 g (0.66 mmoles) of dibenzyl, m.p. 52°, was also isolated and did not lower the melting point when mixed with pure sample. After acidification of salts, 0.4 g (2.94 mmoles) of phenylacetic acid, m.p. 75°, was isolated. Formaldehyde was determined as dimedone derivative, m.p. 188° (according to handbook data: m.p. 189°).

Reaction of phenacylbenzoyl peroxide with freshly plated-out copper in methyl alcohol. A 1.3 g (5.1 mmoles) solution of phenacylbenzoyl peroxide (98% activity) was agitated for 2 hours with 1 g of freshly plated-out copper in 20 ml of absolute methanol. During this time 34 ml (1.52 mmoles) of $CO_2$ was evolved. Using the method described above, we obtained 0.16 g of formaldehyde dimedone derivative, m.p. 188°; 0.16 g (0.88 mmoles) of dibenzyl, m.p. 51° (a sample mixed with pure dibenzyl melted at 52°); 0.61 g of a benzoic – phenylacetic acid mixture. From the neutralization equivalent we determined that the mixture was composed of 67.5% (3.37 mmoles) benzoic and 32.5% (1.47 mmoles) phenylacetic acid. Acidification of salts yielded 0.19 g (1.55 mmoles) of benzoic acid, m.p. 120°. This accounted for 94% of the benzoyloxy radical.

## SUMMARY

1. We investigated reactions of benzoyl, acetylbenzoyl, p-nitrobenzoylbenzoyl, phenacyl, and phenacylbenzoyl peroxides with Na, Zn, Fe, Ni, Cu, Hg, Ag and Pt metals in various solvents.

2. We have established that there are three types of peroxide reactions with metals in alcohols. With some metals formation of metallic salts is observed (Na, Zn, Hg). With other metals (Fe, Ni, Cu, Ag), due to the transfer of a single electron to the peroxide, a $RCOO^-$ anion and a $RCOO\cdot$ radical are formed; the radical then reacts with the solvent. In chloroorganic solvents catalyzed chlorination of the metal is observed. With platinum catalytic hydrogenation of peroxide at the expense of alcohol takes place.

3. A comparison of a benzoyloxy radical reactivity with that of $CH_3COO$, $C_6H_5CH_2COO$, and p-$O_2NC_6H_4COO$ radicals is made.

## LITERATURE CITED

[1] G. A. Razuvaev, Iu. A. Ol'dekop, V. N. Latiaeva, J. Gen. Chem., 26, 1110 (1956).[**]

[2] W. Waters, J. Chem. Soc., 1937, 113.

[3] G. A. Razuvaev, M. M. Koton, J. Gen. Chem. 3, 792 (1933).

[4] M. M. Koton, J. Gen. Chem. 2, 345 (1932).

[5] F. I. Berezovskaia, O. N. Semikhatova, J. Gen. Chem. 6, 114 (1936); 7, 937 (1937).

[6] G. A. Razuvaev, B. N. Moryganov, E. P. Dlin, Iu. A. Ol'dekop, J. Gen. Chem. 24, 262 (1954).[**]

[7] O. A. Reutov, M. A. Besprozvannyi, Proc. Acad. Sci. USSR, 80, 765 (1951).

[8] G. A. Razuvaev, Iu. A. Ol'dekop, J. Gen. Chem. 19, 1487 (1949);[**] G. A. Razuvaev, Iu. A. Ol'dekop, N. S. Viazankin, J. Gen. Chem. 21, 1283 (1951);[**] B. A. Dolgoplosk, B. L. Erusalimskii, V. A. Krol' and L. M. Romanov, J. Gen. Chem. 24, 1775 (1954).[**]

[9] U. Nef, Lieb. Ann. 298, 280 (1897).

[10] P. D. Bartlett and J. E. Leffler, J. Am. Chem. Soc. 72, 3030 (1950).

[11] H. Wieland, T. Ploetz and H. Indest, Lieb. Ann. 532, 166 (1937).

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[*] A. N. Emelianov (student) took part in this experiment.

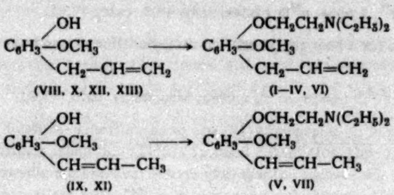
[**] Original Russian pagination. See C.B. translation.

# SYNTHESIS OF SOME ISOMERIC METHOXY-ALLYL-DIETHYL-AMINOETHOXYBENZENES

M. Pal'gi

Some methoxy-allyl-diethylaminoethoxybenzenes possess a styptic action and cause womb contraction [1-3]. According to the literature, out of a number of isomeric methoxy-allyl-diethylaminoethoxybenzenes only the following have been synthesized: 1-methoxy-6-allyl-1-diethylaminoethoxybenzene (I), b.p. 161-163° (12 mm) [1], 140-143° (3-4 mm) [4]; 2-methoxy-4-allyl-1-diethylaminoethoxybenzene (II), b.p. 158° (10 mm) [5]; 4-methoxy-2-allyl-1-diethylaminoethoxybenzene (III), b.p. 166° (6 mm) [6]; 3-methoxy-6-allyl-1-diethylaminoethoxybenzene (IV), b.p. 200-205° (12 mm) [6]; and also a propenyl derivative – 2-methoxy-4-propenyl-1-diethylaminoethoxybenzene (V), b.p. 185-187° (4 mm) [7].

We have improved the synthetic methods for isomers (I, II, III, V) and also synthesized 2-methoxy-3-allyl-1-diethylaminoethoxybenzene (VI) and 2-methoxy-6-propenyl-1-diethylaminoethoxybenzene (VII) for the first time.



$$C_6H_3\begin{cases}OH\\OCH_3\\CH_2-CH=CH_2\end{cases}\longrightarrow C_6H_3\begin{cases}OCH_2CH_2N(C_2H_5)_2\\OCH_3\\CH_2-CH=CH_2\end{cases}$$

(VIII, X, XII, XIII) (I–IV, VI)

$$C_6H_3\begin{cases}OH\\OCH_3\\CH=CH-CH_3\end{cases}\longrightarrow C_6H_3\begin{cases}OCH_2CH_2N(C_2H_5)_2\\OCH_3\\CH=CH-CH_3\end{cases}$$

(IX, XI) (V, VII)

## EXPERIMENTAL

In the synthesis of isomeric methoxy-allyl-diethylaminoethoxybenzenes we started with the corresponding methoxy-allyl phenols. Diethylaminoethyl ethers of the latter were prepared by boiling the phenol for 8-10 hours in absolute alcohol with 2-chlorotriethylamine (used in 25% excess) and sodium ethoxide. The syntheses were carried out under nitrogen atmosphere. To isolate the reaction products we distilled off the alcohol, dissolved the NaCl formed in water, and extracted the methoxy-allyl-diethylaminoethoxybenzene from an alkaline solution with ether. The ether extract was shaken repeatedly with a 10% hydrochloric acid solution. After the acid solution was made alkaline with 10% sodium hydroxide, the methoxy-allyl-diethylaminoethoxybenzene separated out and was extracted with ether; the ether solution was dried over anhydrous sodium sulfate. Following the removal of ether, we distilled the product twice in vacuo at 2-3 mm pressure. The yields and properties of products are listed in the table.

The 2-chlorotriethylamine needed in this synthesis was prepared in the following way: diethylethanolamine was obtained from ethylenechlorohydrin and diethylamine (60% yield) [8] and was chlorinated in chloroform [9-12] or benzene [13] with thionyl chloride. Best results were obtained in chloroform with mechanical stirring at −5 to 0°. Excess thionyl chloride and chloroform were distilled off in vacuum. The 2-chlorotriethylamine hydrochloride was converted into free base. Since the product decomposed on standing [10], it was vacuum-distilled immediately before being used. The yield was 70-85%.

TABLE

| Substances obtained | Yield (in %) | Boiling point (pressure in mm) | $n^{t}D$ | $d^{t}_{4}$ | $MR_D$ (calc. 79.50) | Found N (%) (calc. 5.33%) |
|---|---|---|---|---|---|---|
| 2-Methoxy-6-allyl-1-diethylaminoethoxybenzene (I) . . . . . | 60 | 141-144° (2-3) | $1.5075^{24.5}$ | $0.9842^{24.5}$ | 79.70 | 5.0 |
| 2-Methoxy-6-propenyl-1-diethylaminoethoxybenzene (VII) . . . . | 25 | 120-124 (3) | $1.5265^{24}$ | $0.9852^{24}$ | 82.1 | 5.12 |
| 2-Methoxy-4-allyl-1-diethylaminoethoxybenzene (II) . . . . . | 50 | 150-153 (2-3) | $1.5128^{23}$ | $0.9817^{23}$ | 80.4 | 5.6 |
| 2-Methoxy-4-propenyl-1-diethylaminoethoxybenzene (V) . . . . . | 61 | 159-161 (2) | $1.5358^{20}$ | $0.9956^{20}$ | 82.4 | 5.25 |
| 4-Methoxy-2-allyl-1-diethylaminoethoxybenzene (III) . . . . | 40 | 144-148 (3) | $1.5160^{17}$ | $0.9918^{17}$ | 80.0 | 5.39 |
| 2-Methoxy-3-allyl-1-diethylaminoethoxybenzene (VI). . . . . | 20 | 142-145 (3) | $1.5050^{18}$ | $0.9698^{18}$ | 80.45 | 5.65 |

B. p. 58-60° (30 mm), $n^{22.5}D$ 1.4358, $d^{22.5}_{4}$ 0.9166, $MR_D$ 39.2, calc. 38.72.

The methoxy-allylphenols necessary for the synthesis of methoxy-allyl-diethylaminoethoxybenzenes were obtained in the following manner.

2-Methoxy-6-allylphenol (o-eugenol) (VIII). By starting with guaiacol and allyl bromide we obtained an allyl guaiacol ether [14-16]. The yield was 65%.

B. p. 111-113° (12 mm), $d^{18}_{4}$ 1.0554, $n^{18}D$ 1.5345, $MR_D$ 48.3, calc. 47.61.

When the ether was heated for 1 hour at 210-215° in diethylaniline, 2-methoxy-6-allylphenol [14, 16, 17] was obtained in 80% yield.

B. p. 119-121° (12 mm), $n^{18.5}D$ 1.5410, $d^{18.5}_{4}$ 1.0685, $MR_D$ 48.2; calc. 47.61.

2-Methoxy-6-propenylphenol (o-isoeugenol) (IX) was prepared from o-eugenol by heating with aqueous KOH (1 part KOH, 1 part $H_2O$, 2 parts o-eugenol) for 3.5 hours at 170° [14-16] under a nitrogen atmosphere. B. p. 106-109° (3 mm). After distillation the product immediately crystallized and the unreacted o-eugenol was removed by suction, m.p. 68°. After recrystallization from benzene, m.p. 74°. The yield was 45%.

2-Methoxy-4-allylphenol (eugenol) (X) was extracted with 10% KOH from oil of cloves (Oleum caryphylli) [18, 19]. The yield was 70% of the oil used.

B. p. 122-124° (12 mm), $n^{25}D$ 1.5385, $d^{25}_{4}$ 1.0538, $MR_D$ 48.5; calc. 47.61.

2-Methoxy-4-propenylphenol (isoeugenol) (XI) was prepared from eugenol by heating the latter with KOH and a small amount of water for 10 minutes at 220° under a nitrogen atmosphere [20]. The yield was 85%.

B. p. 128-130° (8 mm), $n^{18}D$ 1.5732, $d^{18}_{4}$ 1.0848, $MR_D$ 49.87; calc. 47.61.

4-Methoxy-2-allylphenol (XII). Methylation of hydroquinone with dimethylsulfate in a NaOH solution at pH 8-9 (at room temp. under $N_2$) gave p-methoxyphenol [21]. Yield was 60%, b.p. 120-123 (8 mm), m.p. 53°. From p-methoxyphenol and allyl bromide we obtained p-methoxyphenyl allyl ether [6]. Synthesis was carried out under $N_2$. Yield was 87%.

B. p. 120° (10 mm), $n^{18}D$ 1.5288, $d^{18}_{4}$ 1.0534, $MR_D$ 48.00; calc. 47.61.

p-Methoxyphenylallyl ether was heated for 30 minutes at 245-250° and gave 4-methoxy-2-allylphenol [6]. The yield was 60%.

B. p. 143-144° (8 mm), $n^{16}D$ 1.5502, $d^{16}_{4}$ 1.0865, $MR_D$ 48.08; calc. 47.61.

The hydroxyl content was determined by acylation in pyridine solution. Found %: OH 10.5; calc. 10.4.

**2-Methoxy-3-allylphenol (XIII).** o-Nitrophenylallyl ether was prepared from o-nitrophenol and allyl bromide [15] in a 90% yield.

B. p. 123-125° (3 mm), $n^{17}D$ 1.5550, $d^{17}_4$ 1.1926, $MR_D$ 48.17; calc. 47.4.

The ether was heated for 5 hours at 180° and produced 2-nitro-6-allylphenol [15]. Synthesis was done under nitrogen; the yield was 65-70%.

B. p. 103-105° (3 mm), $n^{16}D$ 1.5800, $d^{16}_4$ 1.2148, $MR_D$ 49.26; calc. 47.4.

This compound was methylated with dimethylsulfate. The yield of 2-nitro-1-methoxy-6-allylbenzene was 75-80%.

B. p. 110-114° (3 mm), $n^{18}D$ 1.5244, $d^{18}_4$ 1.1480, $MR_D$ 50.3; calc. 50.24.

This product was in turn reduced with alcoholic sodium sulfide. The yield of 1-amino-2-methoxy-3-allylbenzene was 65%.

B. p. 100-104° (3 mm), $n^{18}D$ 1.5550, $d^{18}_4$ 1.0394, $MR_D$ 50.3; calc. 50.15.

Kjeldahl nitrogen determination gave 8.32%; calc. 8.58%. We diazotized 1-amino-2-methoxy-3-allylbenzene and decomposed the diazo compound by dropwise addition of copper sulfate (20 parts $CuSO_4$, 20 parts $(NH_4)_2SO_4$, 10 parts $Na_2SO_4$, 40 parts $H_2O$, 30 parts 50% $H_2SO_4$) at 105-110° (under nitrogen). The 2-methoxy-3-allylphenol was distilled off with superheated steam. The yield was 50%.

B. p. 119-120° (12 mm), $n^{16}D$ 1.5370, $d^{16}_4$ 1.0762, $MR_D$ 47.62; calc. 47.61.

Acylation in pyrdine, to determine hydroxyl groups, gave 10.8%; calc. 10.4%. Active hydrogen (Terent'ev method) was found to be 1.03.

## SUMMARY

1. We established that if alkylation of isomeric methoxy-allylphenols with 2-chlorotriethylamine is carried out under nitrogen there is a marked increase in the yield of the corresponding methoxy-allyl-diethylaminoethoxybenzenes as compared to the same synthesis run in the presence of air; the reaction products are also much purer.

2. Synthetic methods are given for the 2-methoxy-3-allyl-1-diethylaminoethoxybenzene and 2-methoxy-6-propenyl-1-diethylaminoethoxybenzene, both prepared for the first time.

## LITERATURE CITED

[1] Germ. Pat. 433182; Zb., 1926, II, 2223.

[2] A. M. Khaletskii, G. I. Sokolova, J. Gen. Chem., 22, 1648 (1952).

[3] S. Kuroda and S. Koyama, J. Pharm. Soc. Japan, 63, 382 (1943); Ch. A., 1951, 3349.

[4] T. Takahashi and S. Senda, J. Pharm. Soc. Japan, 67, 21 (1947); Ch. A., 1951, 9499.

[5] Austr. Pat. 99678; Zbl., 1926, I, 494.

[6] T. Takahashi and S. Senda, J. Pharm. Soc. Japan, 69, 498 (1949); Ch. A., 1950, 4440.

[7] S. Senda, J. Pharm. Soc. Japan, 70, 561 (1950); Ch. A., 1951, 7976.

[8] Synth. Org. Prep., Coll. 2, 248 (1949).*

[9] G. A. Gough and H. King, J. Chem. Soc., 1928, 2426.

[10] E. Gryszkiewicz-Trochimowski and S. Otolski, Arch. Chemij Farmacij, 2, 171; 3, 215; Zbl., 1935, I, 1876; 1938, II, 306.

[11] Swiss Pat. 190719; Zbl., 1937, II, 3953.

[12] US Pat. 2458823; Ch. A., 1949, 3461.

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*In Russian.

[13] F. Giral, M. L. Cascajares, Escuela nac. ciens. biol. I. P. N. Mexico Ciencia, 5, 105-B (1944); Ch. A. 1947, 4892.

[14] F. Mauthner, J. pr. Chem., 148, 95 (1937).

[15] L. Claisen and O. Eisleb, Lieb. Ann., 401, 50 (1913).

[16] R. S. Livshits, M. S. Bainova, G. I. Veslevskia, E. I. Genkin, N. A. Preobrazhenskii, Iu. M. Rozanova and Z. A. Baranova, J. Gen. Chem.,21, 1354 (1951).*

[17] L. Claisen, Ber., 45, 3161 (1912).

[18] M. Wassermann, Lieb. Ann., 170, 369 (1876).

[19] Erlenmeyer, Z. Chem., 1866, 430.

[20] A. Einhorn and C. Frey, Ber., 27, 2455 (1894).

[21] H. Bredereck, I. Henning and W. Rau, Ber., 86, 1085 (1953).

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# SYNTHESIS OF $\beta$-AMINO ACIDS FROM AROMATIC HYDROXY AND ALKOXYALDEHYDES

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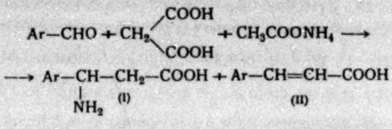
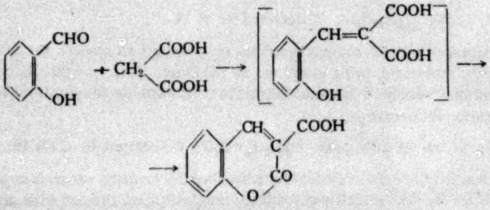
One of us had discovered [1] a convenient method of preparing $\beta$-amino acids by the reaction of aldehydes with malonic acid in the presence of ammonia or ammonium salts; this method has now been extended to aldehydes or aromatic [2], aliphatic [3], alicyclic [4], and heterocyclic [5] series. It has been established that in the case of substituted aromatic aldehydes the yield of $\beta$-amino acids as well as the ability for the reaction itself to proceed depends to a large extent on the nature and position of the substituents. In the present work we have shown data on the reaction of various hydroxy and alkoxyaldehydes with malonic acid, in the presence of ammonium acetate (T. Johnson's modification of V. M. Rodionov's reaction). In the classical case a mixture of two substances is formed in the reaction: $\beta$-amino acid (I) and $\alpha,\beta$-unsaturated acid (II).



$$\mathrm{Ar{-}CHO} + \mathrm{CH_2}\begin{matrix}\diagup\mathrm{COOH}\\ \diagdown\mathrm{COOH}\end{matrix} + \mathrm{CH_3COONH_4} \longrightarrow \longrightarrow \underset{(I)}{\mathrm{Ar{-}\underset{\underset{\displaystyle NH_2}{|}}{CH}{-}CH_2{-}COOH}} + \underset{(II)}{\mathrm{Ar{-}CH{=}CH{-}COOH}}$$

Monohydroxybenzaldehydes. When salicylaldehyde was boiled with malonic acid and ammonium acetate in ethyl alcohol, instead of the corresponding $\beta$-amino acid we obtained coumarin-3-carboxylic acid, probably as a result of cyclization in the intermediate o-hydroxylbenzylidenemalonic acid.



m-Hydroxybenzaldehyde behaved normally giving a mixture of $\beta$-(3-hydroxyphenyl)-$\beta$-alanine (52.6% yield) and 3-hydroxycinnamic acid (9.5% yield). These yields were obtained by carrying out the reaction in n-butyl alcohol. In ethyl alcohol the yield of amino acid was somewhat lower.

When p-hydroxybenzaldehyde, malonic acid, and ammonium acetate reacted in boiling ethyl alcohol, a mixture of two products resulted: diammonium 4-hydroxybenzylidenemalonate (36.5%) and $\beta$-(4-hydroxyphenyl)-$\beta$-alanine (25.5%).

Monomethoxybenzaldehydes. A mixture of o-methoxybenzaldehyde, malonic acid, and ammonium acetate boiled in ethyl alcohol gave only o-methoxycinnamic acid (40% of theoretical yield); the corresponding $\beta$-amino acid was not formed.* In the case of m-methoxybenzaldehyde we obtained a 62.5% yield of β-(3-methoxyphenyl)-β-alanine. Under these conditions p-anisaldehyde gave β-(4-methoxyphenyl)-β-alanine (56%) and 4-methoxycinnamic acid (27%).

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[*] Deceased.

Dihydroxy(methoxy)benzaldehydes. Out of the three investigated representatives of this group (protocatechuic aldehyde, vanillin, veratrib aldehyde) only veratric aldehyde formed a corresponding β-amino acid (52% yield). In the case of protocatechuic aldehyde we obtained 3,4-dihydroxycinnamic acid. Vanillin gave diammonium 3-methoxy-4-hydroxybenzylidenemalonate.

The data presented show that o-hydroxy and o-methoxysubstituted benzaldehydes (which do not form β-amino acids when they react with malonic acid and ammonium acetate) belong to a special group. In all other isomers the yield of β-amino acid from a methoxybenzaldehyde is higher than from a similarly substituted phenolaldehyde.

## EXPERIMENTAL

1) We mixed 5 g of salicylaldehyde, 4.8 g of malonic acid, 7.8 g of ammonium acetate, and 10 ml of ethyl alcohol and boiled them for 3 hours. The precipitate that formed was filtered out with suction, washed with hot alcohol, and when cold, with ether. The yield was 2.6 g, m.p. 205-207°. The substance (ammonium salt) contained nitrogen, was soluble in alkali, and insoluble in acids. Recrystallization from 40% acetic acid gave coumarin-3-carboxylic acid, m.p. 185-187°. No melting point depression was observed when the material was mixed with a known pure sample of the compound. All the efforts to isolate even a small admixture of β-amino acid from the ammonium salt of coumarin-3-carboxylic acid were unsuccessful.

2) n-Hydroxybenzaldehyde was prepared according to Woodward's directions [6]. We boiled a mixture of 25 g of this aldehyde, 24 g of malonic acid, 37.6 g of ammonium acetate, and 49 ml of n-butyl alcohol for 2.5 hours. The precipitate was filtered out, washed with hot alcohol, and when cool, with ether. The yield of β-(3-hydroxyphenyl)-β-alanine was 19.5 g (52.6%). M.p. 222-223° (with decomposition, from 50% alcohol). Further recrystallization did not raise the melting point. Posner [7] gives m.p. 235-236° (with decomp.).

Found %: C 59.67, 60.02; H 6.18, 6.07; N 7.69. $C_9H_{11}O_3N$. Calculated %: C 59.66; H 6.07; N 7.73.

After removal of β-amino acid one could isolate 3-hydroxycinnamic acid from the mother liquor.

3) We boiled 5 g of p-hydroxybenzaldehyde, 4.8 g of malonic acid, 7.5 g of ammonium acetate, and 10 ml of ethyl alcohol for 3 hours. After the reaction was completed, we filtered the precipitate while it was still hot, washed it with hot alcohol, and with ether, after it cooled off. We obtained 2.7 g of material which contained nitrogen, was soluble in alkali and insoluble in acids. M. p. 188-190° (with decompn.). On the basis of composition it was diammonium 4-hydroxybenzylidenemalonate.

Found %: N 11.77, 11.70; $C_{10}H_{14}O_5N_2$. Calculated %: N 11.57.

This substance was heated with 5% sodium hydroxide (to drive off ammonia), the solution was cooled and acidified with dilute hydrochloric acid, using congo red as indicator. The material that precipitated was filtered out with suction and dried in a vacuum dessicator. M.p. 174-175° (with decompn., from water). The substance was analyzed as hydroxybenzylidenemalonic acid.

Found %: C 53.31; 53.52; H 4.62, 4.53. $C_{10}H_8O_5 \cdot H_2O$. Calculated %: C 53.10; H 3.54.

A sample of the dicarboxylic acid obtained was boiled for 2.5 hours in water; during this time we observed the evolution of carbon dioxide. The solution was cooled, the precipitate filtered with suction and dried. M. p. 194-195° (from water). We did not detect any melting point depression when this substance was mixed with pure p-coumaric acid. Thus, the main reaction product (36.5% yield) was diammonium 4-hydroxybenzylidenemalonate.

After this was removed, 1.8 g of the nitrogen-containing material precipitated from the mother liquor during the next 2 days; it was soluble in acids and alkali. M.p. 173-174.5° (with decompn., from a 1 : 1 water – alcohol mixture). The melting point did not change after further recrystallization. The yield of β-(4-hydroxyphenyl)-β-

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* It should be pointed out that one of us together with A. M. Fedorova [2] had obtained β-(2-methoxyphenyl)-β-alanine hydrochloride by running the reaction in alcoholic ammonia solution.

-alanine (β-tyrosine) was 25.5%. Posner [7] reports m.p. 196°.

Found %: C 59.40, 59.51; H 6.26, 6.19; N 7.71, 7.79. $C_9H_{11}O_3N$. Calculated %: C 59.66; H 6.07; N 7.73.

O,N-Dibenzoyl derivatives of β-tyrosine were obtained using Schotten-Baumann benzoylation method. M.p. 194-194.5° (with decompn., from 20% alcohol).

Found %: N 3.94, 4.11. $C_{23}H_{19}O_5N$. Calculated %: N 3.60.

4) 2-Methoxybenzaldehyde was prepared according to literature data [8]. We boiled 5 g of this aldehyde, 4.64 g of malonic acid, 7.46 g of ammonium acetate, and 10 ml of ethyl alcohol for 5 hours. No β-amino acid precipitated. Addition of water resulted in precipitation of β-methoxycinnamic acid. M. p. 183-184° (from alcohol).

5) 3-Methoxybenzaldehyde was prepared according to Pschorr's directions [9]. We boiled 2.46 g of this aldehyde, 2.34 g of malonic acid, 3.44 g of ammonium acetate, and 5 ml of ethyl alcohol for 5 hours. The precipitated β-(3-methoxyphenyl)-β-alanine was filtered out, washed with alcohol and ether. The yield was 2.2 g (62.2%). M. p. 216° (with decompn., from 50% alcohol). According to literature data: m.p. 216° (with decompn.). [7].

Found %: C 61.88; H 6.54; N 6.90. $C_{10}H_{13}O_3N$. Calculated %: C 61.53; H 6.66; N 7.18.

6) A mixture containing 10 g of anisaldehyde (4-methoxybenzaldehyde), 7.8 g of malonic acid, 15 g of ammonium acetate, and 20 ml of alcohol was boiled for 9 hours. The precipitate was filtered out with suction while still hot, washed with hot alcohol, and with ether, after it cooled. The yield of β-(4-methoxyphenyl)-β-alanine was 8 g (56%). M. p. 228° (with decompn.). According to literature data: m.p. 232° (T. Johnson [2]).

We were able to isolate 4-methoxycinnamic acid from the mother liquor after distilling off part of the solvent.

7) We boiled 5 g of protocatechuic aldehyde (3,4-dihydroxybenzaldehyde), 4.9 g of malonic acid, 5.58 g of ammonium acetate, and 10 ml of ethyl alcohol for 5 hours. No precipitate of β-amino acid was observed. Acidification gave 2.4 g of 3,4-dihydroxycinnamic acid, m.p. 194-195° (from water).

8) A mixture containing 5 g of vanillin, 4.27 g of malonic acid, 6.35 g of ammonium acetate, and 10 ml of n-butyl alcohol was boiled for 5 hours. A precipitate formed, was filtered out, washed with alcohol and ether. The substance obtained was soluble in water and gave off ammonia when dissolved in 2 N sodium hydroxide. On the basis of composition it corresponded to diammonium 3-methoxy-4-hydroxybenzylidenemalonate. M.p. 193-193.5° (with decompn.). The yield was 3.6 g (40%).

Found %: C 48.24; H 5.91; N 10.17. $C_{11}H_{16}O_6N_2$. Calculated %: C 48.56; H 5.88; N 10.29.

Hydrochloric acid (1 : 1) was added dropwise to a 2.1 g solution of this diammonium salt in 12 ml of 2 N sodium hydroxide. We obtained 1.9 g of 3-methoxy-4-hydroxybenzylidenemalonic acid. M. p. 212° (with decompn., from water).

Found %: C 55.21, 55.61; H 4.43, 4.69. $C_{11}H_{10}O_6$. Calculated %: C 55.46; H 4.20.

When acetylated with acetic anhydride, it gave an O-acetyl derivative. M. p. 173° (with decompn., from water).

Found %: C 55.67; H 4.41. $C_{13}H_{12}O_7$. Calculated %: C 55.71; H 4.28.

9) We boiled 3.8 g of veratric aldehyde (3,4-dimethoxybenzaldehyde), 3.41 g of malonic acid, 4.4 g of ammonium acetate, and 8 ml of n-butyl alcohol for 4 hours. The precipitated β-(3,4-dimethoxyphenyl)-β-alanine was filtered out, washed with alcohol and ether. The yield was 2.68 g (52%). M.p. 221.5-222° (with decompn., from water).

Found %: C 58.43, 58.35; H 6.92, 6.95; N 5.96, 5.98. $C_{11}H_{15}O_4N$. Calculated %: C 58.66; H 6.67; N 6.22.

We were able to isolate 3,4-dimethoxycinnamic acid, m.p. 180-181° (from alcohol), from the mother liquor.

We added 2 ml of acetic anhydride dropwise at 5-10° to 2 g of β-(3,4-dimethoxyphenyl)-β-alanine dissolved in 17 ml of 10% sodium hydroxide. Mixing was continued until the smell of acetic anhydride disappeared (~1 hour);

the solution was then acidified with hydrochloric acid (1 : 1) to a congo red end-point. We obtained 2.55 g of N-acetyl-β-(3,4-dimethoxyphenyl)-β-alanine, m.p. 169-170° (from alcohol).

Found %: C 58.11; H 6.80; N 5.07, 5.34. $C_{13}H_{17}O_5N$. Calculated %: C 58.42; H 6.36; N 5.24.

## SUMMARY

The behavior of isomeric hydroxy- and methoxy-benzaldehydes in V.M. Rodionov's reaction (T. Johnson's modification) was investigated. We established the following.

1. Salicylaldehyde gave coumarin-3-carboxylic acid instead of a β-amino acid. m-Hydroxybenzaldehyde formed β-(3-hydroxyphenyl)-β-alanine in a 52.3% yield. p-Hydroxybenzaldehyde gave a mixture of diammonium 4-hydroxybenzylidenemalonate (36.5% yield) and β-tyrosine (25.5% yield).

2. Among the respective methoxy aldehydes, meta and para isomers gave β-amino acids, while o-methoxybenzaldehyde only an α,β-unsaturated acid.

3. Out of the three disubstituted benzaldehydes, protocatechuic, vanillin, and veratric aldehydes, only the last one formed a β-amino acid.

4. Unique behavior was noted among ortho-substituted benzaldehydes which did not give the corresponding β-amino acids under the conditions of V.M. Rodionov's reaction. In all other cases, methoxybenzaldehydes give a higher yield of β-amino acids than corresponding similarly substituted phenol aldehydes.

## LITERATURE CITED

[1] W. Rodionov and E. Malevinskaja, Ber., 59, 2952 (1926).

[2] W. Rodionov. and A. Fedorova, Ber., 60, 804 (1927); Arch. Pharm., 266, 116 (1928); T. Johnson and J. Livak, J. Am. Chem. Soc., 58, 299 (1936).

[3] V. M. Rodionov, V. K. Zvorykina, Bull. Acad. Sci. USSR, Chem. Sci. Section, 1943, 216.

[4] V. M. Rodionov, T. S. Kiseleva, Bull. Acad. Sci. USSR, Chem. Sci. Section, 1952, 278.*

[5] V. P. Mamaev, N. N. Suvorov, E. M. Rokhlin, Proc. Acad. Sci. USSR, 101, 269 (1955).

[6] Synth. Org. Prep., Coll. 3, 363 (1952).**

[7] T. Posner, Lieb. Ann., 389, 1 (1912).

[8] C. Hell and A. Hofmann, Ber., 38, 1676 (1905).

[9] R. Pschorr, and B. Jäckel, Ber., 33, 1826 (1900).

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**In Russian.

# TRIAROXYISOPHOSPHAZOACYLS OF AROMATIC SERIES

A. V. Kirsanov and G. I. Derkach

Triaroxyisophosphazoacyls of the type $RC(OR')=NPO(OR')_2$ have recently been prepared by the following reaction:

$$RCCl=NPOCl_2 + 3NaOR' \longrightarrow 3NaCl + RC(OR')=NPO(OR')_2, \quad (I)$$

for

$$R=CCl_3,\ R'=C_6H_5,\ \alpha\text{-}C_{10}H_7,\ 1,4\text{-}ClC_{10}H_6\ [1];\ R=(C_6H_5)_2CCl,\ R'=\alpha\text{-}C_{10}H_7 \text{ and}$$
$$R=p\text{-}NO_2C_6H_4,\ R'=\alpha\text{-}C_{10}H_7\ [2].$$

Thus, only five triaroxyisophosphazoacyls were known, of which four were either vitreous substances or thick liquids, and only the last one crystalline. On the basis of such meager material it was impossible to make any deductions concerning the general applicability of reaction (I) or general properties of triaroxyisophosphazoacyls.

In a previous work [3] we described a general method for making trichloroisophosphazoacyls or aromatic series; this enabled us to find within what limits reaction (I) was applicable to the synthesis of triaroxyisophosphazoacyls. It turned out that the reaction is generally applicable to aromatic compounds. We obtained good yields of 22 triaroxyisophosphazoacyls and 1 trimethoxyisophosphazoacyl (see the experimental part and Table 1).

The aromatic series of triaroxyisophosphazoacyls have properties which differ sharply from those of isomeric triaroxyphosphazoacyls [4] as well as from those of the trichloroacetic acid series [1, 2]. The aromatic triaroxyisophosphazoacyls are crystalline, relatively low-melting solids distillable without decomposition in high vacuum. When heated under atmospheric pressure or low vacuum they gradually undergo carbonization (complete decomposition at 320-350°) which is not accompanied by formation of triarylphosphates (in contrast with isomeric triaroxyphosphazoacyls). Therefore, we can conclusively assume that reaction

$$ArC(OR) = NHPO(OR)_2 \xrightarrow{\text{heat}} OP(OR)_3$$

does not take place. Consequently, when phosphazo- and isophosphazoacyl derivatives of carboxylic acids are thermally cleaved, oxygen "jumps over" very readily [4, 5], chlorine somewhat less readily [3], and aroxy groups not at all. For this reason thermal cleavage of phosphazo- and isophosphazo compounds can be used to elucidate their structures.

Triaroxyisophosphazoacyls of aromatic series are comparatively stable towards saponification. They do not hydrolyze in boiling water, but will saponify readily and quantitatively only when boiled with water – alcohol solutions of alkali hydroxides; the reaction proceeds according to the equation

$$ArC(OAr')=NPO(OAr')_2 + 2NaOH \longrightarrow Ar'ONa + H_2O + ArCONNaPO(OAr')_2 \quad (II)$$

Thus, triaroxyisophosphazoacyls behave approximately the same way as triaroxyphosphazosulfonyl compound [6]. Triaroxyisophosphazoacyls saponify incomparably slower than isomeric triaroxyphosphazoacyls [4], or triaroxyisophosphazo- and triaroxyphosphazoacyls of trichloroacetic acid series [1, 2].

It should be noted that the aromatic series of triaroxyisophosphazoacyls are incomparably harder to saponify than isomeric triaroxyphosphazoacyls, while, on the other hand, in the trichloroacetic acid series triaroxyisophosphazoacyls are noticeably easier to saponify than isomeric triaroxyphosphazoacyls, i.e., $ArC(OAr')=NPO(OAr')_2$

TABLE 1

Triaroxyisophosphazoacyls of Type ArC(OR)N=PO(OR)$_2$, Obtained as in Equation (I).

| R | Ar | Yield (in %) | Crystal form, crystallized form | Melting point | Found % N | Gross formula | Calc. % N |
|---|---|---|---|---|---|---|---|
| $C_6H_5$ | $C_6H_5$ | 84.3 | Prisms, benzene + petroleum ether | 100—102° | 3.55 | $C_{25}H_{20}O_4NP$ | 3.26 |
| $C_6H_5$ | $\alpha$-$C_{10}H_7$ | 65.5 | Needles, ether | 97—98 | 3.01 | $C_{29}H_{22}O_4NP$ | 2.92 |
| $C_6H_5$ | o-$ClC_6H_4$ | 95.0 | Prisms, benzene | 119—120 | 2.86 | $C_{25}H_{19}O_4NPCl$ | 3.02 |
| $C_6H_5$ | 2,4-$Cl_2C_6H_3$ | 78.4 | Prisms, petroleum ether | 99—101 | 2.73 | $C_{25}H_{18}O_4NPCl_2$ | 2.81 |
| $C_6H_5$ | m-$NO_2C_6H_4$ | 82.5 | Prisms, petroleum ether, $CCl_4$ | 122—123 | 5.75 | $C_{25}H_{19}O_6N_2P$ | 5.90 |
| $C_6H_5$ | p-$NO_2C_6H_4$ | 80.0 | Prisms, benzene | 139—141 | 6.18 | $C_{25}H_{19}O_6N_2P$ | 5.90 |
| $C_6H_5$ | 3,5-$(NO_2)_2C_6H_3$ | 89.2 | Prisms, petroleum ether, $CCl_4$ | 105—108 | 8.24 | $C_{25}H_{18}O_8N_3P$ | 8.09 |
| $C_6H_5$ | 2,4-$ClNO_2C_6H_3$ | 81.6 | Needles, benzene + petroleum ether | 112—114 | 5.59 | $C_{25}H_{18}O_6N_2PCl$ | 5.50 |
| m-$CH_3C_6H_4$ | p-$NO_2C_6H_4$ | 50.0 | Prisms, benzene, petroleum ether | 113—115 | 5.59 | $C_{28}H_{25}O_6N_2P$ | 5.42 |
| $\alpha$-$C_{10}H_7$ | $C_6H_5$ | 68.5 | Ditto | 146—148 | 2.48 | $C_{37}H_{26}O_4NP$ | 2.42 |
| $\beta$-$C_{10}H_7$ | p-$ClC_6H_4$ | 55.3 | Prisms, petroleum ether | 115—117 | 2.29 | $C_{37}H_{25}O_4NPCl$ | 2.28 |
| p-$ClC_6H_4$ | $C_6H_5$ | 63.4 | Ditto | 107—109 | 2.70 | $C_{25}H_{17}O_4NPCl_3$ | 2.62 |
| p-$ClC_6H_4$ | o-$ClC_6H_4$ | 85.0 | Prisms, benzene | 161—163 | 2.40 | $C_{25}H_{16}O_4NPCl_4$ | 2.47 |
| p-$ClC_6H_4$ | 2,4-$Cl_2C_6H_3$ | 82.4 | Prisms, benzene + petroleum ether | 107—109 | 2.30 | $C_{25}H_{15}O_4NPCl_5$ | 2.32 |
| p-$ClC_6H_4$ | m-$NO_2C_6H_4$ | 68.3 | Prisms, ether, petroleum ether | 119—121 | 4.80 | $C_{25}H_{16}O_6N_2PCl_3$ | 4.85 |
| p-$ClC_6H_4$ | p-$NO_2C_6H_4$ | 73.7 | Prisms, benzene | 152—153 | 4.75 | $C_{25}H_{16}O_6N_2PCl_3$ | 4.85 |
| p-$ClC_6H_4$ | 3,5-$(NO_2)_2C_6H_3$ | 84.5 | Plates, benzene + petroleum ether | 151—153 | 6.71 | $C_{25}H_{15}O_8N_3PCl_3$ | 6.74 |
| o-$NO_2C_6H_4$ | 2,4-$Cl_2C_6H_3$ | 79.9 | Prisms, benzene | 107—109 | 8.70 | $C_{25}H_{15}O_{10}N_4PCl_2$ | 8.84 |
| o-$NO_2C_6H_4$ | p-$NO_2C_6H_4$ | 95.3 | Ditto | 162—163 | 11.53 | $C_{25}H_{16}O_{12}N_5P$ | 11.49 |
| p-$NO_2C_6H_4$ | 2,4-$Cl_2C_6H_3$ | 79.0 | Prisms, dioxane | 147—149 | 8.76 | $C_{25}H_{15}O_{10}N_4PCl_2$ | 8.84 |
| p-$NO_2C_6H_4$ | p-$NO_2C_6H_4$ | 92.3 | Ditto | 220—222 | 11.61 | $C_{25}H_{16}O_{12}N_5P$ | 11.49 |
| p-$NO_2C_6H_4$ | m-$NO_2C_6H_4$ | 82.2 | Ditto | 167—169 | 11.60 | $C_{25}H_{16}O_{12}N_5P$ | 11.49 |
| $CH_3$ | 3,5-$(NO_2)_2C_6H_3$ | 63.8 | Needles, benzene + petroleum ether | 96—98 | 12.85 | $C_{10}H_{12}O_8N_3P$ | 12.61 |

TABLE 2

Diaryl Esters of Acylamidophosphoric Acids of Type ArCONHPO(OR)$_2$, Obtained as in Equation (II)

| R | Ar | Yield (in %) | Crystal form | Melting point | Found % N | Found sapon. equiv. | Gross formula | Calc.* % N |
|---|---|---|---|---|---|---|---|---|
| $C_6H_5$ | $C_6H_5$ | 50.0 | Needles | 147—149° | Sec.[7] | | | |
| $C_6H_5$ | α-$C_{10}H_7$ | 52.0 | Ditto | 127—129 | 3.53 | 0.98 | $C_{23}H_{18}O_4NP$ | 3.47 |
| $C_6H_5$ | o-$ClC_6H_4$ | 61.6 | Prisms | 102—104 | 3.55 | 1.00 | $C_{19}H_{15}O_4NPCl$ | 3.61 |
| $C_6H_5$ | 2,4-$Cl_2C_6H_3$ | 66.4 | Plates | 136—138 | 3.41 | 1.01 | $C_{19}H_{14}O_4NPCl_2$ | 3.32 |
| $C_6H_5$ | m-$NO_2C_6H_4$ | 71.7 | Prisms | 166—167 | 6.92 | 1.00 | $C_{19}H_{15}O_6N_2P$ | 7.03 |
| $C_6H_5$ | p-$NO_2C_6H_4$ | 75.2 | Needles | 151—152 | Sec.[7] | | | |
| $C_6H_5$ | 3,5-$(NO_2)_2C_6H_3$ | 90.4 | Ditto | 197—199 | 9.55 | 0.98 | $C_{19}H_{14}O_8N_3P$ | 9.47 |
| $C_6H_5$ | 2,4-$ClNO_2C_6H_3$ | 93.4 | Ditto | 107—109 | 6.50 | 0.98 | $C_{19}H_{14}O_6N_2PCl$ | 6.47 |
| m-$CH_3C_6H_4$ | p-$NO_2C_6H_4$ | 70.1 | Prisms | 131—133 | 6.57 | 1.02 | $C_{21}H_{19}O_6N_2P$ | 6.56 |
| α-$C_{10}H_7$ | $C_6H_5$ | 84.1 | Tablets | 195—196 | Sec.[7] | | | |
| β-$C_{10}H_7$ | p-$ClC_6H_4$ | 85.5 | Prisms | 165—167 | 3.04 | 1.02 | $C_{27}H_{19}O_4NPCl$ | 2.86 |
| p-$ClC_6H_4$ | $C_6H_5$ | 81.0 | Needles | 131—133 | Sec.[7] | | | |
| p-$ClC_6H_4$ | o-$ClC_6H_4$ | 87.0 | Plates | 179—180 | 3.12 | 0.98 | $C_{19}H_{13}O_4NPCl_3$ | 3.07 |
| p-$ClC_6H_4$ | 2,4-$Cl_2C_6H_3$ | 89.9 | Needles | 152—154 | 2.90 | 1.02 | $C_{19}H_{12}O_4NPCl_4$ | 2.85 |
| p-$ClC_6H_4$ | m-$NO_2C_6H_4$ | 91.4 | Prisms | 171—173 | 6.05 | 1.00 | $C_{19}H_{13}O_6N_2PCl_2$ | 6.00 |
| p-$ClC_6H_4$ | p-$NO_2C_6H_4$ | 73.3 | Ditto | 175—176 | Sec.[7] | | | |
| p-$ClC_6H_4$ | 3,5-$(NO_2)_2C_6H_3$ | 82.7 | Needles | 216—217 | 8.30 | 0.97 | $C_{19}H_{12}O_8N_3PCl_2$ | 8.20 |
| o-$NO_2C_6H_4$ | 2,4-$Cl_2C_6H_3$ | 84.2 | Prisms | 170—171 | 8.28 | 0.98 | $C_{19}H_{12}O_8N_3PCl_2$ | 8.20 |
| o-$NO_2C_6H_4$ | p-$NO_2C_6H_4$ | 83.1 | Ditto | 178—179 | Sec.[7] | | | |
| p-$NO_2C_6H_4$ | 2,4-$Cl_2C_6H_3$ | 83.4 | Ditto | 160—162 | 8.31 | 0.97 | $C_{19}H_{12}O_8N_3PCl_2$ | 8.20 |
| p-$NO_2C_6H_4$ | p-$NO_2C_6H_4$ | 92.4 | Needles | 178—179 | Sec.[7] | | | |
| p-$NO_2C_6H_4$ | m-$NO_2C_6H_4$ | 86.2 | Ditto | 176—178 | 11.62 | 0.97 | $C_{19}H_{13}O_{10}N_4P$ | 11.48 |
| $CH_3$ | 3,5-$(NO_2)_2C_6H_3$ | 95.0 | Ditto | 189—191 | 13.40 | 1.01 | $C_9H_{10}O_8N_3P$ | 13.16 |

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* Calculated equiv. for all the esters = 1.

are relatively hard to saponify, approximately the same as $RSO_2N{=}PCOR'$) (boiling in water – alcohol alkali solutions); $ArCON{=}P(OAr')_3$ are incomparably easier to saponify (shaking with water, heating in 96% ethyl alcohol); $CCl_3CON{=}P(OAr)_3$ saponify in approximately the same way as the preceding one; $CCl_3C(OAr){=}NPO(OAr)_2$ are exceptionally easy to saponify (brief contact with water, storage in air).

As a rule solubilities and melting points of triaroxyisophosphazoacyls depend more on the nature of the three ester groups than on the aryl group connected to the carboxylic carbon atom.

## EXPERIMENTAL

*Preparation of triaroxyisophosphazoacyls as in equation (I). Triphenoxyisophosphazoacyls.* To 0.02 moles of trichloroisophosphazoacyl dissolved in 30.0 ml of $C_6H_6$ we rapidly added 0.0604 moles of dry powdered sodium phenoxide suspended in 10-15 ml of dioxane; this was accompanied by vigorous stirring. The reaction mixture became quite hot because of reaction heat. Stirring was continued until the acid gave neutral reaction with congo red; tests were done on samples containing 2-3 drops of water to 1 ml of reaction mixture. Usually, after 5-10 minutes stirring, the acidity disappeared, but in some cases the mixture had to be refluxed for 10-15 minutes. To remove sodium chloride the reaction mixture was washed with water (2 × 30 ml), the benzene solution dried over sodium sulfate, and benzene distilled off under vacuum. The residue was a solid crystalline mass or a thick oil which crystallized when we added 1-2 ml of petroleum ether to it and rubbed with a glass rod. Triphenoxyisophosphazoacyls were highly soluble in acetone, $C_6H_6$, less soluble in $CCl_4$, ether, and petroleum ether. Tri-n--toloxyisophosphazo-p-nitrobenzoyl was obtained in the same way and had the same solubility properties.

*Tri-α-naphthoxyisophosphazoacyls.* A 0.01 mole trichloroisophosphazoacyl solution in 40 ml of ether was slowly poured into a freshly prepared 0.03 mole solution of sodium α-naphthoxide in 70 ml of ether. The warm solution was stirred for 10-15 minutes and cooled to + 10°; the crystalline precipitate was filtered with suction and contained the reaction product mixed with sodium chloride. To remove the latter we washed the precipitate with water (5 × 3 ml), then with ethyl alcohol (2 × 2 ml) and ether (2 × 3 ml). Tri-α-naphthoxyisophosphazoacyls are sparingly soluble in $C_6H_6$, $CCl_4$, and ether, very sparingly in alcohol and petroleum ether.

*Tri-p-chlorophenoxyisophosphazoacyls.* A solution containing 0.02 moles of trichloroisophosphazoacyl in 40 ml of $C_6H_6$ was mixed with 0.0604 moles of sodium p-chlorophenoxide suspended in 40 ml of ether. The warm solution was stirred and (if necessary) refluxed until it gave a neutral reaction in the test with water. While sodium chloride was washed away with water (2 × 30 ml), a large part of the reaction product (60-70%) precipitated in a crystalline form. To remove the substance more completely the solvents were distilled off under vacuum. Tri--p-chlorophenoxyisophosphazoacyls are fairly soluble in acetone, much less in $C_6H_6$, $CCl_4$, ether, and petroleum ether.

*Trinitrophenoxyisophosphazoacyls.* To 0.0605 moles of carefully dried powdered sodium o- or p-nitrophenoxide we added 0.02 g of trichloroisophosphazoacyl dissolved in 40-50 ml $C_6H_6$; addition was made all at once and the mixture refluxed with stirring until an aqueous sample gave neutral reaction with congo red (this usually required 1.5-3.5 hours). After the mixture cooled to room temperature, the isophosphazo compound that precipitated was filtered out with suction, washed with hot water (6 × 5 ml) to remove sodium chloride, then with ethyl alcohol (2 × 5 ml) and ether (4 × 5 ml) to remove free nitrophenol. Trinitrophenoxyisophosphazoacyls are sparingly soluble in dioxane, acetone, $C_6H_6$, ethyl alcohol, ether, $CCl_4$, and insoluble in pertoleum ether.

*Trimethoxyisophosphazo-3,5-dinitrobenzoyl.* We cooled a 0.045 mole solution of sodium methoxide in 40 ml of methanol to 0° and added to it 0.015 moles of trichloroisophosphazo-3,5-dinitrobenzoyl dissolved in 40 ml of $C_6H_6$; addition was carried out with vigorous stirring and at such a rate as would maintain the temperature of reaction mixture between 0 and 5°. Then, the mixture was heated to boiling and allowed to cool; sodium chloride was removed by centrifugation and the solvents distilled off in vacuum. The liquid residue quickly crystallized after we added 2 ml of petroleum ether, 2 ml of ether and rubbed it with a glass rod. Trimethoxyisophosphazo--3,5-dinitrobenzoyl is slightly soluble in $C_6H_6$, acetone, methanol, much less in petroleum ether, $CCl_4$, and ether.

*Diaryl esters of acylamidophosphoric acids obtained from hydrolysis of triaroxyisophosphazoacyls as in equation (II).* A mixture containing 0.001 moles of triaroxyisophosphazoacyl, 60 ml of ethyl alcohol, and 10 ml of 2 N aqueous sodium hydroxide was refluxed for one hour. Meanwhile the solid completely dissolved. We distilled off ethyl alcohol in vacuum and added 5 ml of water plus 5 N hydrochloric acid until the solution became acid to congo red. At the same time the diesters came out of solution as oils which soon crystallized. They were filtered with suction, washed with water (2 x 5 ml), ethyl alcohol (2 x 1 ml) and recrystallized. All the diesters of acylamidophosphoric acid were soluble in acetone, slightly soluble in ether, ethyl alcohol, $C_6H_6$ and rather insoluble in $CCl_4$ and petroleum ether. Diesters of acylamidophosphoric acids are weak monobasic acids, and form readily water-soluble salts with alkali hydroxides. Analytical data and melting points are given in Table 2.

## SUMMARY

Action of sodium aroxides on trichloroisophosphazoacyls of aromatic series produced triaroxyisophosphazoacyls; their properties are described.

It was demonstrated that during thermal cleavage of triaroxyisophosphazoacyls the aroxy group could not split out to give triarylphosphates.

Alkaline saponification of triaroxyisophosphazoacyls yielded diaryl esters of acylamidophosphoric acids of aromatic series; their properties are described.

## LITERATURE CITED

[1] A. V. Kirsanov and G. I. Derkach, J. Gen. Chem. 26, 2631 (1956);* 27, 1080 (1957).*

[2] A. V. Kirsanov and G. I. Derkach, J. Gen. Chem. 27, 3248 (1957).*

[3] A. V. Kirsanov and G. I. Derkach, J. Gen. Chem. 28, 1887 (1958).*

[4] A. V. Kirsanov, G. I. Derkach, and R. G. Makitra, J. Gen. Chem. 28, 1227 (1958).*

[5] A. V. Kirsanov, Bull. Acad. Sci. USSR Div. Chem. Sci. 1954, 649;* A. V. Kirsanov, R. G. Makitra, J. Gen. Chem., 26, 907 (1956).*

[6] A. V. Kirsanov, and V. I. Shevchenko, J. Gen. Chem. 24, 882, 1980 (1954).*

[7] A. V. Kirsanov and R. G. Makitra, J. Gen. Chem. 27, 245 (1957).*

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*Original Russian pagination. See C.B. translation.

# SOME β,β-DIARYLETHYLAMINES

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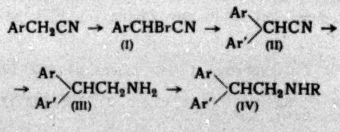
A series of fatty aromatic amines possess a high pharmacological activity, and some of them have found practical medicinal use. Derivatives of β-phenylethylamine and its branched homologs constitute a large and important group in this class of compounds. At the same time, there is almost no information in the chemical literature about the physiological activity of β,β-diarylethylamines. Some cyclic analogs of these compounds (containing piperidine ring) show great stimulating action on the central nervous system [1]. In connection with this, it was interesting to discover the pharmacological activity of some β,β-diarylethylamine derivatives, and in particular, of N-alkyl-β,β-diarylethylamines.

The synthesis of compounds we were interested in was carried out as in equation

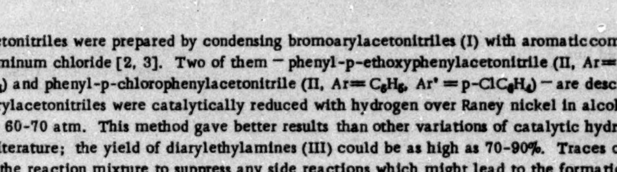


$$ArCH_2CN \rightarrow \underset{(I)}{ArCHBrCN} \rightarrow \underset{(II)}{(Ar)(Ar')CHCN} \rightarrow \underset{(III)}{(Ar)(Ar')CHCH_2NH_2} \rightarrow \underset{(IV)}{(Ar)(Ar')CHCH_2NHR}$$

Diarylacetonitriles were prepared by condensing bromoarylacetonitriles (I) with aromatic compounds in the presence of aluminum chloride [2, 3]. Two of them – phenyl-p-ethoxyphenylacetonitrile (II, Ar= $C_6H_5$, Ar' = = p-$C_2H_5OC_6H_4$) and phenyl-p-chlorophenylacetonitrile (II, Ar= $C_6H_5$, Ar' = p-$ClC_6H_4$) – are described for the first time. Diarylacetonitriles were catalytically reduced with hydrogen over Raney nickel in alcoholic solution at 45-70° under 60-70 atm. This method gave better results than other variations of catalytic hydrogenation described in the literature; the yield of diarylethylamines (III) could be as high as 70-90%. Traces of alcoholates were placed in the reaction mixture to suppress any side reactions which might lead to the formation of secondary amines.

In the synthesis of previously unknown N-alkyl-β,β-diarylethylamines (IV) the greatest difficulties were encountered in the last step (monoalkylation of a primary amino group). Direct alkylation with alkyl halides in the presence of alkali gave mainly tertiary amines; when a deficiency of alkylating material was used, we obtained complicated mixtures containing secondary and tertiary amines together with original primary, and it was very difficult to separate the secondary amine. Unsatisfactory results were also obtained in alkylation with dialkylsulfates and in alkylation of p-toluylsulfonyl derivatives of β,β-diarylethylamines.

The method of Späth and Bruck [4] gave the best results in the preparation of N-methyl-β,β-diarylethylamines (65-75% yield); this method involved the alkylation of corresponding anil derivatives with alkyl halides and subsequent hydrolysis of N-methyl bases.



$$(III) \xrightarrow{C_6H_5CHO} (Ar)(Ar')CHCH_2N{=}CHC_6H_5 \xrightarrow{CH_3I} (Ar)(Ar')CHCH_2\overset{CH_3}{\underset{I^-}{N^+}}{=}CHC_6H_5 \xrightarrow{H_2O} (Ar)(Ar')CHCH_2NHCH_3$$

However, when this method was applied to make N-alkyl derivatives with larger radicals, it did not give the desired product. When the amine was alkylated with ethyl bromide, the yield of N-ethyl derivative was insignificant; higher alkyl halides gave completely negative results.

To obtain N-alkyl-β,β-diarylethylamines with radicals larger than methyl, we catalytically alkylated primary amines with respective alcohols by heating them in the presence of Raney nickel [5]; this was applied for the first time to alkylation of aliphatic amines. This method proved to be convenient enough and enabled us to prepare N-isoamyl-β,β-diphenyl-, N-ethyl-β-phenyl-β-p-chlorophenyl-, and N-ethyl-β-phenyl-β-p-ethoxyphenylethylamine in a 35-90% yield.

We prepared also a few representative N,N-dialkyl-β,β-diarylethylamines so as to compare the pharmacological activities of monoalkyl derivatives with those of corresponding tertiary amines. These were synthesized in the usual way (direct alkylation of corresponding β,β-diarylalkylamines with alkyl halides in the presence of alkali).

The N-alkyl-β,β-diarylethylamines we obtained were colorless, oily liquids, stable in storage. They formed easily-crystallizing hydrochlorides. In some cases picrates were also made to characterize the amines.

β,β-Diarylethylamine (III), N-alkyl-β,β-diarylethylamine (IV), and N,N-dialkyl-β,β-diarylethylamine hydrochlorides were tested for their physiological activity by N. A. Kruglov in the pharmacological section of the Institute. They all were inferior to phenocoll in their stimulating action on the central nervous system; compounds (III) ($Ar = C_6H_5$, $Ar' = p\text{-}ClC_6H_4$ and $p\text{-}C_2H_5C_6H_4$) approached phenocoll in activity. Compounds of type (III) and (IV) showed weak antihistamine activity and weak anesthetic action.

## EXPERIMENTAL

Diphenylacetonitrile (50% yield, m.p. 72-74°), phenyl-p-tolylacetonitrile (50% yield, m.p. 60°) and phenyl-p-methoxyphenylacetonitrile (15% yield, b.p. 170-172° at 2 mm) were obtained by known methods [3].

*Phenyl-p-ethoxyphenylacetonitrile.* To a solution containing bromobenzyl cyanide (prepared from 59 g of benzyl cyanide and 88 g of bromine and used without separation) and 300 g of phenetole in 135 ml of nitrobenzene we gradually added 66 g of aluminum chloride at 50°; the mixture was then heated for 2 hours at 110°, left at room temperature for 24 hours, frozen and treated with concentrated hydrochloric acid and extracted with ether; the extract was washed with a sodium carbonate solution and water, then dried over sodium sulfate. The solvent was distilled off and the residue vacuum-distilled; we collected the 160-195° (at 1 mm) fraction which crystallized completely in the receiver. The yield was 24.5 g (20% computed from benzyl cyanide), m.p. 89-90° (from ethyl alcohol).

Found %: C 81.08, 81.18; H 6.43, 6.46; N 5.74, 5.82. $C_{16}H_{15}ON$. Calculated %: C 81.01; H 6.75; N 5.90.

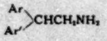
*Phenyl-p-chlorophenylacetonitrile.* was similarly obtained from 59 g of benzyl cyanide, 88 g of bromine, and 300 g of chlorobenzene in 135 ml of nitrobenzene plus 66 g of aluminum chloride. The yield was 33 g (25%), b.p. 170-171° at 3 mm, m.p. 74-78° (from ethyl alcohol).

Found %: N 6.01, 5.88; Cl 15.39, 15.43. $C_{14}H_{10}NCl$. Calculated %: N 6.22; Cl 15.58.

*Diarylethylamines.* Concentrated methanol solution of diarylacetonitrile was hydrogenated at 60-70 atm. and 40-50° in the presence of Raney nickel (50% by weight of nitrile used) until absorption of hydrogen stopped (usually 2-3 hours). Before hydrogenation we added 0.1-0.25 g of sodium to the solution. We filtered away the catalyst, added dilute hydrochloric acid until the mixture became acidic and distilled off the alcohol in vacuum. The aqueous acidic solution was washed with ether, made strongly basic with alkali hydroxide, and extracted with ether; the extract was dried over sodium sulfate, the solvents distilled off, and the residue distilled in vacuum. Hydrochloride was prepared by saturating an ether solution of the amine with anhydrous hydrogen chloride and purified by precipitating with ether from alcohol or acetone. The data on compounds obtained are compiled in Table 1.

*N-Methoyl-β,β-diarylethylamine.* We heated 1 mole of β,β-diarylethylamine with 1.2 moles of benzaldehyde for 0.5 hours over a water bath and distilled off in vacuum (at temperature not in excess of 50°) the water produced; we then added 1.2 moles of methyl iodide and heated the mixture for 10-12 hours on a water bath at 70°. After the solution cooled, we added 30-40 ml of methanol, 5 ml of water and refluxed for 15-20 minutes;

TABLE 1

β,β-Diarylethylamines 
$\begin{matrix}Ar\\Ar'\end{matrix}\!>CHCH_2NH_2$

| No. of exp. | Ar | Ar' | Hydrogenation Pressure (atm.) | Hydrogenation Temperature | Yield (in °C) | Boiling point (pressure in mm) | Melting point | $n_D^{20}$ | $d_4^{20}$ | % N Found | % N Calculated | Melting point of hydrochloride | % Cl Found | % Cl Calculated |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $C_6H_5$ | $C_6H_5$ | 60 | 47° | 89 | 155—156° (6) | 44—45°* | | | 7.09, 7.22 | 7.11 | 263° | 14.89, 14.98 | 14.96 |
| 2 | $C_6H_5$ | p-$CH_3C_6H_4$ | 60 | 50 | 70 | 152—153 (3) | — | 1.5551 | 1.0404 | 6.29, 6.48 | 6.44 | 225—227 | 14.26, 14.51 | 14.20 |
| 3 | $C_6H_5$ | p-$C_2H_5OC_6H_4$ | 65 | 40 | 76 | 164—165 (5) | 39—40 | — | — | 5.62, 5.65 | 5.91 | 173** | 12.73, 12.73 | 12.76 |
| 4 | $C_6H_5$ | p-$CH_3OC_6H_4$ | 65 | 40 | 70 | 170—172 (5) | — | 1.5875 | 1.0890 | 6.13, 6.41 | 6.45 | 188*** | 13.43, 13.54 | 13.49 |
| 5 | $C_6H_5$ | p-$ClC_6H_4$ | 65 | 40 | 40 | 160—164 (2) | — | 1.5962 | 1.1405 | 6.12, 6.13 | 6.30 | 210**** | 13.42, 13.53 | 13.34 |

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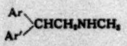
* According to literature data [2]: m.p. 38°, b.p. 149° at 4 mm.

** Picrate m.p. 182-183°.

*** Picrate m.p. 168-172°.

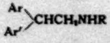
**** Picrate m.p. 199-201°.

TABLE 2

N-Alkyl-β,β-diarylethylamines 
$\begin{matrix}Ar\\Ar'\end{matrix}\!>CHCH_2NHCH_3$

| No. of exp. | Ar | Ar' | Yield (in %) | Boiling point (pressure in mm) | $n_D^{20}$ | % N Found | % N Calculated | Melting point of hydrochloride | % Cl Found | % Cl Calculated |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $C_6H_5$ | $C_6H_5$ | 45.2 | 150—151° (5) | 1.5809 | 6.50, 6.53 | 6.56 | 216—217° | 14.09, 14.33 | 14.11 |
| 2 | $C_6H_5$ | p-$CH_3C_6H_4$ | 50 | 150—151 (3) | 1.5841 | 5.76, 5.87 | 6.21 | 130—133 | 13.41, 13.48 | 13.53 |
| 3 | $C_6H_5$ | p-$C_2H_5OC_6H_4$ | 50 | 163—164 (3) | 1.5442 | 5.68, 5.85 | 5.50 | 132—133 | 11.97, 11.98 | 12.12 |
| 4 | $C_6H_5$ | p-$CH_3OC_6H_4$ | 58 | 167—170 (3) | 1.5771 | 5.87, 5.93 | 5.84 | Oil | —, — | — |
| 5 | $C_6H_5$ | p-$ClC_6H_4$ | 65.5 | 161—163 (3) | — | 5.85, 6.05 | 5.67 | 142 | 12.74, 12.84 | 12.51 |

TABLE 3

N-Alkyl-β,β-diarylethylamines  $\overset{Ar}{\underset{Ar'}{>}}CHCH_2NHR$

| No. of exp. | Ar | Ar' | R | Yield (in %) | Boiling point (pressure in mm) | $n_D^{20}$ | % N |  | Melting point of hydrochloride | % Cl |  |
|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  |  | Found | Calculated |  | Found | Calculated |
| 1 | $C_6H_5$ | $C_6H_5$ | iso-$C_5H_{11}$ | 35* | — | — | — — | — | 186—177° | 11.70, 11.89 | 11.67 |
| 2 | $C_6H_5$ | p-$ClC_6H_4$ | $C_2H_5$ | 50 | 145—155°(3) | 1.5661 | 5.76, 5.83 | 5.43 | 144—145 | 11.93, 11.96 | 11.96 |
| 3 | $C_6H_5$ | p-$CH_3OC_6H_4$ | $C_2H_5$ | 55 | 165 (5) | — | 5.42, 5.56 | 5.44 | — | — — | — |

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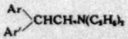
* Isolated as hydrochloride.

TABLE 4

N,N-Dialkyl-β,β-diarylethylamines  $\overset{Ar}{\underset{Ar'}{>}}CHCH_2N(C_2H_5)_2$

| No. of exp. | Ar | Ar' | Yield (in %) | Boiling point (pressure in mm) | $n_D^{20}$ | % N |  | Melting point of hydrochloride | % Cl |  |
|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  | Found | Calculated |  | Found | Calculated |
| 1 | $C_6H_5$ | $C_6H_5$ | 90 | 140—142° (2) * | — | 5.94, 5.81 | 5.52 | 144—145° | 12.30, 12.20 | 12.23 |
| 2 | $C_6H_5$ | p-$ClC_6H_4$ | 89 | 197—198 (14) | 1.5661 | 4.84, 5.05 | 4.87 | — | — — | — |
| 3 | $C_6H_5$ | p-$C_2H_5OC_6H_4$ | 50 | 190—191 (9) | 1.5456 | 5.13, 5.12 | 4.98 | 96—102 | 11.00, 11.02 | 11.08 |
| 4 | $C_6H_5$ | p-$CH_3C_6H_4$ | 71 | 165—170 (4) | 1.5551 | 5.11, 4.94 | 5.24 | 136—137 | 11.64, 11.72 | 11.33 |

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* According to literature data [6]: b.p. 189-190° at 22 mm; hydrochloride, m.p. 149°.

the benzaldehyde was then steam-distilled, the residue acidified with acetic acid, neutral products extracted with ether, and the aqueous layer made basic with alkali hydroxides; the base separating-out was extracted with ether, dried, and distilled in vacuum.

Hydrochlorides were made by passing anhydrous hydrogen chloride through an ether solution of amine. Purification was done by precipitating from acetone with ether. The data on compounds obtained are compiled in Table 2.

N-Alkyl-β,β-diarylethylamines. We heated 1 mole of β,β-diarylethylamine in a 10-fold excess of suitable alcohol for 12-14 hours (with stirring over a water bath) in the presence of Raney nickel (50% by weight of amine used). After the mixture cooled, the catalyst was filtered away, alcoholic solution dried, alcohol distilled off, and the reaction product vacuum-distilled. Hydrochlorides were prepared and purified in a way already described. The data on compounds obtained are compiled in Table 3.

N,N-Dialkyl-β,β-diarylethylamines. Alkyl bromide (2.2 moles) was added gradually (and with stirring) to a mixture of β,β-diarylethylamine (1 mole) and 8% aqueous sodium hydroxide (3 moles); the reaction mixture was then heated for 2 hours. It was left standing at room temperature for 24 hours, after which the base was extracted with ether. The ether solution was dried over sodium sulfate, the ether distilled off and the reaction product vacuum-distilled. Hydrochlorides were prepared and purified in the usual way. The data on the compounds prepared are compiled in Table 4.

## SUMMARY

1. A series of N-alkyl-β,β-diarylethylamines were prepared.

2. Methylation of corresponding anils with methyl iodide was used in monoalkylation of β,β-diarylalkylamines. Monoalkyl derivatives with larger radicals were prepared by catalytic alkylation of primary amines with alcohols in the presence of Raney nickel.

## LITERATURE CITED

[1] J. Heer, E. Sury, and K. Hoffmann, Helv. Chim. Acta, 38, 134 (1955).

[2] R. Funke, Bull. Soc. Chim., (5), 16, 241 (1949).

[3] D. Shapiro, J. Am. Chem. Soc., 71, 839 (1949).

[4] E. Spāth, I. Bruck, Ber., 70, 2446 (1937).

[5] R. Rice and E. Kahn, J. Am. Chem. Soc., 77, 4052 (1955).

[6] M. Kharash and G. Glapp, J. Org. Ch., 3, 355 (1938).

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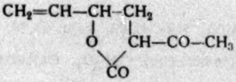
# RESEARCH IN THE FIELD OF UNSYMMETRICAL ORGANIC α-OXIDES

## XVII. REACTION OF PENTADIENYL OXIDE WITH ETHYL SODIOACETOACETATE

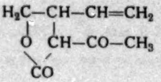
F. G. Ponomarev and Iu. M. Mosichkin

Continuing our investigation of various chemical transformations of pentadiene oxides [1], we are reporting in this work the experimental results on the condensation of ethyl sodioacetoacetate with 1,2-epoxypentene-3 (I), and 2,3-epoxypentene-4 (II). The products of these reactions (unsaturated γ-lactones) have not been described in the literature before. Besides, they might be of considerable physiological interest, in analogy with other active compounds containing butyrolactone groupings [2-4].

We know from the literature, that when ethyl sodioacetoacetate adds to 1,2-epoxybutene-3, it does so to a large extent against Markownikoff's rule, forming two isomeric lactones (a) and (b) whose structure has been proven [5].

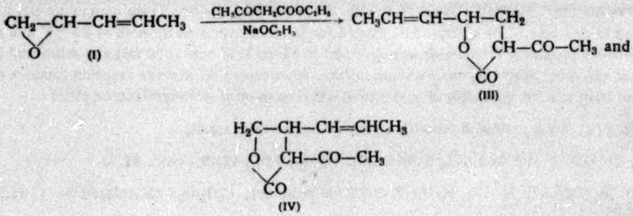


and



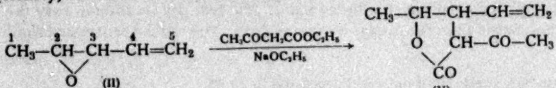
(a) (b)

When 1,2-epoxypentene-3 (I) was condensed with ethyl sodioacetoacetate just as in the case of 1,2-epoxybutene-3, we expected to get a mixture of lactones which have been assigned the structures of α-aceto-γ-propenyl-γ-butyrolactone (III) and α-aceto-β-propenyl-γ-butyrolactone (IV) in analogy with the pentene case.



(I) (III) (IV)

Since the reactivity of a primary carbon atom in the ring of the studied oxide is greater than that of a secondary (similar to other unsymmetrical oxides [6]), one would consequently expect a predominant formation of lactone (III). However, in the case of 2,3-epoxypentene-4 (II) reaction with ethyl sodioacetoacetate, the main product seemed to be α-acetyl-β-vinyl-γ-methyl-γ-butyrolactone (V) formed through the action of reagent anion on the most reactive (tertiary) carbon atom of the oxide (II).



(II) (V)

The presence and location of a double bond in lactone (V) was determined by oxidation with potassium permanganate. Formic acid was shown to be present among the oxidation products.

## EXPERIMENTAL

Pentadiene oxides (I) and (II) needed in this investigation were prepared from pentadiene by a previously described method and had the following properties:

(I) – b.p. 82-84°, $d^{20}_4$ 0.8465, $n^{20}D$ 1.4129, $MR_D$ 24.78; calc. 24.26.

(II) – b.p. 104-106°, $d^{20}_4$ 0.8768, $n^{20}D$ 1.4339, $MR_D$ 24.85; calc. 24.26.

These constants are practically identical with the ones listed in the literature [1, 7, 8].

Reaction of 1,2-epoxypentene-3- (I) with ethyl sodioacetoacetate. We added 14 g of freshly distilled ethyl acetoacetate (b.p. 68-69° at 10 mm, $n^{20}D$ 1.4208) to an alcoholic solution of sodium ethoxide (3 g of sodium in 44 ml of absolute ethyl alcohol). Next, we gradually added 8.4 g of 1,2-epoxypentene-3 with stirring. Evolution of heat was observed which raised the temperature from 0 to 50° and the mixture acquired a deep-red coloration. After the addition of oxide was completed, a reflux condenser with a calcium chloride tube was attached to the flask and the mixture heated for 6 hours in a water bath at 50-60°. A few hours later a solid snow-white sodium derivative of the lactone precipitated out. The next day, ethyl alcohol was distilled off under reduced pressure, and the colored amorphous residue was dissolved (the flask had to be cooled with ice water) in 150 ml of 35% acetic acid. The resulting solution was saturated with sodium chloride, extracted many times with ether, and the ether extract dried over anhydrous sodium sulfate. Ether was driven off and the residue distilled in vacuum. We obtained 10 g of condensation products (120-155° fraction at 8 mm) from which after subsequent two-fold fractionation we isolated about 1 g of α-aceto-γ-propenyl-γ-butyrolactone (III) (with admixture of (IV)) in the form of a light-yellow oil with a pleasant smell.

B. p. 152-155° at 8 mm, $d^{20}_4$ 1.1211, $n^{20}D$ 1.4671, $MR_D$ 41.62; calc. 41.79.

Found %: C 64.34; H 6.83. M 167.5, 170.1 (in benzene), $C_9H_{12}O_3$. Calculated %: C 64.27; H 7.16. M 168.2.

It was highly soluble in ether, acetone, ethyl acetoacetate, not so much in water. It rapidly decolorized aqueous bromine and potassium permanganate solutions.

Reaction of 2,3-epoxypentene-4 (II) with ethyl sodioacetoacetate. We added 16.8 g of freshly distilled ethyl acetoacetate and 10 g of 2,3-epoxypentene-4 (II) to an alcoholic solution of sodium ethoxide (3.6 g of sodium in 53 ml of absolute ethyl alcohol). In contrast with the preceding reaction (with compound (I)) no evolution of heat was observed in this case. The mixture was heated for 12 hours over a water bath at 50-60° and the alcohol driven off under reduced pressure; the residue was dissolved in 5% sulfuric acid (300 ml) and extracted with ether; the ether extract was dried over anhydrous sodium sulfate, ether driven off and the reaction product vacuum-distilled. We obtained from this 3.1 g (15.5%) of α-aceto-β-vinyl-γ-methyl-γ-butyrolactone (V).[*]

Lactone (V) was a yellowish oil with a pleasant peppermint smell.

B. p. 126-126.5° at 8 mm, $d^{20}_4$ 1.0764, $n^{20}D$ 1.4585, $MR_D$ 42.43; calc. 41.79.

Found %: C 65.07; H 7.25, M 165.9, 169.2 (in benzene). $C_9H_{12}O_3$. Calculated %: C 64.27; H 7.16. M 168.2.

It was highly soluble in ether, benzene, acetone, ethylacetoacetate, sparingly in water. It rapidly decolorized and aqueous solution of bromine or potassium permanganate. It dissolved in aqueous ammonia and could be recovered unchanged on acidification.

Oxidation of lactone (V) with potassium permanganate. To a 2 g lactone solution in 5 ml of acetone we added 55 ml of 5% water–acetone potassium permanganate solution (dropwise over a period of 3 hours) while the solution was being stirred and cooled with ice water. The next day we filtered away the manganese dioxide and distilled off the acetone from the filtrate on a water bath. The residue contained formic acid, which when warmed up with mercuric chloride precipitated white calomel, m.p. 301°, and with silver nitrate formed a black silver deposit.

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[*] If dissolved in 35% acetic acid the yield decreased to 10.5%.

## SUMMARY

Products obtained in the reaction of 1,2-epoxypentene-3 and 2,3-epoxypentene-4 with ethyl sodioacetoacetate are described.

## LITERATURE CITED

[1] F. G. Ponomarev, O. G. Kharenko and M. F. Shavkova, J. Gen. Chem., 27, 1226 (1957).*

[2] N. Houben, Organic Chemistry Methods, III, 2nd ed. 2, 180 (1935).**

[3] M. M. Shemiakin and A. S. Khokhlov, The Chemistry of Antibiotics (1953).***

[4] R. Goldstein, Chemical Petroleum Processing IL (1952).**

[5] R.M. Adams and C. A. Vander Werf, J. Am. Chem. Soc., 72, 4368 (1950).

[6] A. A. Petrov, Problems in Chemical Kinetics, Catalysis, and Reactivity, AN SSSR, 785 (1955);*** Heterocyclic Compounds, Vol. 1, IL (1953).**

[7] A. N. Pudovik and B. E. Ivanov, J. Gen. Chem. 26, 2771 (1956).*

[8] A. N. Pudovik and B. E. Ivanov, Proc. Acad. Sci. USSR, 103, 443 (1955).

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*Original Russian pagination. See C.B. translation.

**Russian translation.

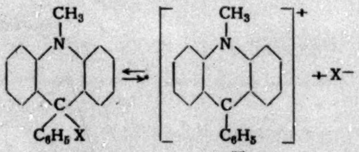
***In Russian.

# DISSOCIATION OF ARYLCARBINOLS AND SOME OTHER COMPOUNDS IN NITROBENZENE. II

**E. I. Kviat**

In a preceding communication [1], using conductometric and spectrophotometric methods, we studied the dissociation of malachite green and crystal violet dyes, as well as their amine base, carbinol base, and methyl ether derivatives. In the present work we have investigated the dissociation of acridine bases conductometrically.

Experiments were conducted on 9-phenyl-10-methylacridinium iodide (I), 9-phenyl-10-methyl-9-hydroxy-9,10-dihydroacridine (II), and on the methyl ether of the latter (III). We found out that all these compounds also dissociated in nitrobenzene solutions, where the dissociation of covalent compounds resulted in the formation of 9-phenyl-10-methylacridinium cations (I'), as shown in the equation below.



(I')

where X = I (I), OH (II), $OCH_3$ (III)

As may be seen in Table 1, the electrical conductance of (I) did not change on standing (constant conductance was observed over a period of a year). After dilution, the equilibrium was established almost instantaneously and the changes in specific conductance were approximately proportional to dilution. Thus, 9-phenyl-10-methylacridinium iodide as well as malachite green and crystal violet behaved like strong electrolytes in nitrobenzene [1].

The limiting equivalent conductance of compound (I) is $\lambda^0 = 34\ \text{ohm}^{-1} \cdot \text{cm}^2$. It was determined by extrapolation to infinite dilution. The limiting ion conductance of organic cation (I') was calculated from the above-listed value for compound (I) and the limiting iodide ion conductance ($\lambda^0_{I^-} = 20\ \text{ohm}^{-1} \cdot \text{cm}^2$) [13]. The calculated value for compound (I') was $\lambda^0 = 14\ \text{ohm}^{-1} \cdot \text{cm}^2$. The value obtained was approximately 2 times larger than the limiting conductance of malachite green and crystal violet cations [1].

With compounds (II) and (III) we observed a gradual increase in conductance on standing and a nonproportional conductance change with dilution; the same had been observed with carbinol bases and other covalent derivatives of crystal violet and malachite green. A particularly large increase in conductance was observed during the first 15 days. We were unable to attain an equilibrium state.

We were unable to determine the degree of dissociation of acridine derivatives spectrophotometrically and calculate from it the limiting equivalent conductance (as was done for malachite green), since the $\lambda_{max}$ of acridine derivatives was too close to that of nitrobenzene. The limiting conductance of acridine derivatives was calculated by summing up the conductance of organic cation (I') and that of the respective anions. In a preceding communication [1] we determined the values for $OH^-$ and $CH_3O^-$ ions, $\lambda^0_{OH^-} = \lambda^0_{CH_3O} = 17.5\ \text{ohm}^{-1} \cdot \text{cm}^2$. We obtained $\lambda^0 = 31.5\ \text{ohm}^{-1} \cdot \text{cm}^2$ for the limiting equivalent conductance of carbinol and methoxy acridine

TABLE 1

Conductance of Compounds (I), (II), and (III) in Nitrobenzene

| Concentration (m) | Days | (I) | | (II) | | (III) | |
|---|---|---|---|---|---|---|---|
| | | $\varkappa \cdot 10^5$ | $\lambda$ | $\varkappa \cdot 10^6$ | $\lambda$ | $\varkappa \cdot 10^6$ | $\lambda$ |
| $10^{-2}$ | 1 | 25.3 | 25.3 | 1.62 | 0.16 | 2.65 | 0.26 |
| | 2 | 25.3 | 25.3 | 3.48 | 0.35 | 3.50 | 0.35 |
| | 5 | 25.3 | 25.3 | 4.28 | 0.43 | 4.6 | 0.46 |
| | 8 | 25.3 | 25.3 | 5.0 | 0.50 | 5.1 | 0.51 |
| | 10 | 25.3 | 25.3 | 5.12 | 0.51 | 5.25 | 0.52 |
| | 15 | 25.3 | 25.3 | 5.53 | 0.55 | 5.77 | 0.58 |
| | 90 | 3 | 25.3 | 12.54 | 1.25 | 11.5 | 1.15 |
| $2 \cdot 10^{-3}$ | 1 | 6.1 | 30.5 | 1.58 | 0.79 | 2.52 | 1.12 |
| | 2 | 6.1 | 30.5 | 2.3 | 1.15 | 2.71 | 1.35 |
| | 5 | 6.1 | 30.5 | 2.82 | 1.41 | 3.26 | 1.62 |
| | 8 | 6.1 | 30.5 | 3.16 | 1.58 | 3.35 | 1.67 |
| | 15 | 6.1 | 30.5 | 3.54 | 1.72 | 3.75 | 1.87 |
| | 90 | 6.1 | 30.5 | 9.4 | 4.7 | 8.1 | 4.05 |
| $4 \cdot 10^{-4}$ | 1 | 1.3 | 32.5 | 1.45 | 3.62 | 1.16 | 2.9 |
| | 2 | 1.3 | 32.5 | 1.95 | 4.88 | 1.64 | 4.1 |
| | 5 | 1.3 | 32.5 | 2.25 | 5.6 | 1.86 | 4.62 |
| | 8 | 1.3 | 32.5 | 2.50 | 6.25 | 2.1 | 5.25 |
| | 15 | 1.3 | 32.5 | 2.67 | 7.16 | 2.54 | 6.3 |
| | 90 | 1.3 | 32.5 | 4.5 | 11.2 | 4.4 | 11.0 |

TABLE 2

| Concentration (moles/liter) | Degree of dissociation $\alpha$ (in %) | | |
|---|---|---|---|
| | (I) | (II) | (III) |
| $10^{-2}$ | 89 | 4.1 | 3.8 |
| $2 \cdot 10^{-3}$ | 98 | 15.5 | 13.3 |
| $4 \cdot 10^{-4}$ | 100 | 36.5 | 35.8 |

derivatives. In view of the fact that we were unable to attain an equilibrium state for compounds (II) and (III), the degree of dissociation was computed for the conductance data obtained on the 90th day after dilution (Table 2). Therefore, as one would expect, the dissociation constants of acridine derivatives calculated from these values differed considerably from each other at different concentrations. The dissociation constant of acridinium iodide was $K = 4 \times 10^{-2}$, and free energy $\Delta F_0^\circ = 1770$ kcal/ mole. The degree of dissociation and dissociation constants of compounds (I), (II), and (III) in nitrobenzene were determined by the approximate Debye and Onsager method [3] with the help of Schedlovsky's tables [4].

I wish to express my deepest thanks to O.F. Ginzburg for his valuable suggestions.

## EXPERIMENTAL

Conductance determinations were done using a method described in a preceding communication [1]. Compounds (I), (II), and (III) were synthesized according to literature data [2].

Observations on the change of conductance in solutions were carried out over a period of few months from the time of their preparation. Solutions studied were prepared through successive dilutions. The solutions were alternately diluted on the fifteenth day after preparation.

## SUMMARY

1. It was determined that 9-phenyl-10-methylacridinium iodide acts as a strong electrolyte in nitrobenzene solution. Conductance change is proportional to dilution. Dissociation is instantaneous. Dissociation of 9-phenyl-10-methyl-9-hydroxy-9,10-dihydroacridine and of its methyl ether takes place slowly and increases with dilution.

2. We have calculated the limiting equivalent conductances of 9-phenyl-10-methylacridinium iodide, 9-phenyl-10-methyl-9-hydroxy-9,10-dihydroacridine and of its methyl ether, and also of 9-phenyl-10-methylacridinium cation in nitrobenzene solutions.

3. We have calculated the degree of dissociation of acridine derivatives at different concentrations in nitrobenzene, and also the dissociation constant of 9-phenyl-10-methylacridinium iodide.

## LITERATURE CITED

[1] E. I. Kviat, O. F. Ginzburg, J. Gen. Chem. 28, 51 (1958).*

[2] G. Dekker, J. Russ. Phys. Chem. Soc. 26, 265 (1894).

[3] S. Glasstone, Introduction to Electrochemistry [Russ. trans.], IL, 133, 221-225 (1951).

[4] R. M. Fuoss and T. Schedlovsky, J. Am. Chem. Soc., 71, 1496 (1949); 73, 4977 (1951).

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# REACTIONS OF AROMATIC NITRO COMPOUNDS

## IV. TRANSALKYLATION OF 2,4-DINITROPHENOLIC ETHERS

S. S. Gitis, M. S. Malinovskii and A. I. Glaz

We have recently shown that a methoxy group in 2,4-dinitroanisole can easily be replaced with other alkoxy groups at room temperature [1]. We presumed that the mechanism of this reaction was similar to that of trinitroanisole with alcoholates [2], according to which, when alcoholic alkali reacts with 2,4-dinitroanisole, they form an intensely colored intermediate of quinoid structure, one similar to the intermediate quinoid complex proposed by Bevan and Bye [3] in their work on methoxylation of mono- and dinitrofluorobenzenes.

In the present work we have discussed the peralkylation not only of 2,4-dinitroanisole, but also of other alkyl ethers of 2,4-dinitrophenol.

We established a rule, that when one group replaced another, the alkoxy group with the most negative inductive effect would be displaced.

TABLE 1

| Amount of KOH (in moles) per 1 mole of 2,4-dinitroanisole. | Melting point of unrecrystallized product. | Yield (in %) |
|---|---|---|
| 1.0 | 67-70° | 82 |
| 1.5 | 72-75 | 85 |
| 2.0 | 75-78 | 85 |
| 2.5 | 79-81 | 87 |
| 3.0 | 80-83 | 90 |
| 3.5 | 82-84 | 90 |
| 4.0 | 83-85 | 90 |
| 5.0 | 79.5-81 | 90 |

We found out, that the following could be prepared in good yields through peralkylation: 2,4-dinitroanisole from 2,4-dinitrophenyl β-hydroxyethyl ether, 2,4-dinitrophenol from 2,4-dinitroanisole, 2,4-dinitrophenyl n-propyl ether from 2,4-dinitrophenetole, 2,4-dinitrophenyl n-butyl ether from 2,4-dinitrophenyl n-propyl ether, 2,4-dinitrophenyl primary-isobutyl ether from 2,4-dinitrophenyl n-butyl ether, 2,4-dinitrophenyl primary-isoamyl ether from 2,4-dinitrophenyl primary-isobutyl ether. On the other hand, 2,4-dinitroanisole could not be prepared from 2,4-dinitrophenetole, etc. Therefore, we could arrange the alkoxy groups in the order of their "replacing power," just as is shown below

$$\text{primary-iso-}C_5H_{11}O > \text{primary-iso-}C_4H_9O > n\text{-}C_4H_9O > n\text{-}C_3H_7O >$$
$$> C_2H_5O > CH_3O > HOCH_2CH_2O$$

The series fully agreed with the data on the acidity of alkoxyacetic acids [4].

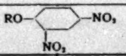
The investigated peralkylation reaction took place at room temperature in one hour. These were the optimum conditions. If the solutions were left standing for a longer or shorter period of time, the yield and the quality of products were lowered. The amount of alcoholic alkali used was very important. We used 4 moles of alkali per 1 mole of ether. If less alkali were used, incomplete conversion took place resulting in a mixture of two ethers. This can be seen in the case where 2,4-dinitroanisole was converted into 2,4-dinitrophenetole, as shown in Table 1.

Trans-etherification was carried out under completely different conditions by Ogata and Ocano [5]. They have shown that a methoxy group, a glycol radical, or a phenoxy group could be replaced by other alkoxy groups when heated under pressure or refluxed for many hours with appropriate alcoholic solutions of 2,4-dinitroanisole and 0.25 moles of potassium hydroxide. Under those conditions, they succeeded in preparing glycolic ether of 2,4-dinitrophenol from 2,4-dinitroanisole; this, as we have pointed out above, could not be done with excess alkali at room temperature. All this gave us reason to believe that the peralkylation followed a different mechanism under different conditions.

## EXPERIMENTAL

We dissolved 0.01 moles of starting alkyl ether in 20 ml of benzene. To this solution we added 0.04 moles of potassium hydroxide dissolved in 20 ml of the appropriate alcohol for the ether. The colored solution was shaken for five minutes and left standing for 1 hour. Subsequently, we added 50 ml of water to the solution, whereupon the color changed to straw-yellow. The benzene solution was washed three times with water to remove excess alkali and potassium 2,4-dinitrophenoxide which was formed in a side reaction. The ethers remained in the residue after benzene was distilled off. Solid ethers were recrystallized from ethyl alcohol, while liquid ones distilled in vacuo. Experimental results are shown in Table 2.

TABLE 2

|  |  | Yield (in %) | Melting point |  |
|---|---|---|---|---|
| R in the starting ether | R in the final ether |  | Our data | Literature data [6] |
| $HOCH_2CH_2$ | $CH_3$ | 96 | 94-95* | 95* |
| $CH_3$ | $C_2H_5$ | 87 | 85-86 | 86 |
| $C_2H_5$ | n-$C_3H_7$ | 89 | 29.5-30 | 30.5-31 |
| n-$C_3H_7$ | n-$C_4H_9$ | 90 | B.p. 161.5-162 (0.1 mm) | 178-180 (2 mm) |
| n-$C_4H_9$ | $(CH_3)_2CHCH_2$ | 89 | 30 | 30.3-31.5 |
| $(CH_3)_2CHCH_2$ | primary-iso-$C_5H_{11}$ | 90 | B.p. 168-170 (0.2 mm) | 175-178 (1 mm) |

## SUMMARY

1. Peralkylation of 2,4-dinitrophenolic ethers can be carried out at room temperature in the presence of potassium hydroxide.

2. We have arranged the alkoxides in order to their substituting power; this order is related to the values of the negative inductive effect.

## LITERATURE CITED

[1] S. S. Gitis and A. I. Glaz, J. Gen. Chem. 28, 1334 (1958).*

[2] S. S. Gitis and A. I. Glaz, J. Gen. Chem. 27, 1897 (1957).*

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*Original Russian pagination. See C.B. translation.

[3] C. W. L. Bevan and C.C. Bye, J. Chem. Soc. 1954, 3091,

[4] M. H. Paloma, Zbl., 1912, II, 596.

[5] I. Ogata, Ch. A 45, 5123 (1951); I. Ogata and M. Ocano, Ch. A. 46, 1487, 4500 (1952); J. Am. Chem. Soc., 71, 3211 (1949).

[6] J. Wesson, J. Am. Chem. Soc., 62, 3466 (1940).

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# ADDITION OF HYDROGEN HALIDES TO ESTERS OF α,β-UNSATURATED ACIDS

V. N. Mikhailov and V. V. Pigulevskii

It is known that esters of acrylic and methacrylic acids can add halogen halides to form the corresponding esters of β-halopropionic and β-halobutyric acid [1-3]. We found out in a preceding work [3] that to obtain these esters the absorption of hydrogen chloride had to be carried out with cooling, and the process would only be completed after the reaction mixture had sat at room temperature (10-15 hours).

Although quite a large number of esters of the above-mentioned acids had been prepared (synthesized by various methods [3-6]), their properties have been studied very little, and therefore, their possible practical applications are to a large degree still unknown at the present. Esters of β-halopropionic acid can be used in the synthesis of 1-phenyl-3-pyrazolidone [7], which is beginning to be widely applied in photographic processes for speeding the developing [8].

In this communication we have described the synthesis of butyl esters by β-chloro(bromo, iodo)-propionic and butyric acids by the addition of respective hydrogen halides to butyl esters of acrylic and methacrylic acids. Properties of the synthesized esters are listed in Table 1. Butyl esters of β-iodopropionic and β-chloro(iodo)-isobutyric acids have been prepared for the first time.

All the synthesized esters of the above-mentioned acids are colorless, transparent, mobile liquids with a fairly strong odor. In the absence of light they are all completely stable at room temperature and remain colorless on prolonged standing. They can be distilled without decomposition at reduced pressure, but will partially decompose at atmospheric pressure forming corresponding esters of acrylic and methacrylic acids; these in turn, will spontaneously undergo polymerization in the absence of inhibitors. The esters are highly soluble in ethyl alcohol, plain diethyl ether, and acetone.

The described synthetic method may be used to obtain other esters of β-halopropionic and β-haloisobutyric acids, due to its simplicity and good yields.

## EXPERIMENTAL

Synthesis of butyl ester of β-chloropropionic acid. This ester was obtained by a method we had previously worked out for the methyl ester of β-chloropropionic acid [3]. Cooled butyl acrylate (0°) was placed in a glass test tube and anhydrous hydrogen chloride was passed through it until complete saturation (1 : 1 molar ratio) was achieved; this was measured by increase in weight. The time needed to saturate the compound was 1-1.5 hours. The reaction mixture was kept in a covered test tube at room temperature for 10-15 hours, then fractionally distilled at reduced pressure. After a two-fold fractionation we collected the 89-91° (at 5 mm) fraction; its constants agreed with those listed in the literature for butyl ester of β-chloropropionic acid [1, 3, 4]. The yield of the ester was 88-90% (Table 2).

Synthesis of butyl ester of β-chloroisobutyric acid. The experiment was performed similarly to the previous one. Duration of saturation was 1.5-2 hours. After a two-fold fractionation at reduced pressure, we collected the 89-92° (at 10 mm) fraction which corresponded to the butyl ester of β-chloroisobutyric acid. Yield of the ester was 78-80% (Table 3).

Synthesis of butyl esters of β-bromopropionic and β-bromoisobutyric acids. Butyl esters of acrylic and

TABLE 1

The Properties of Butyl Esters of β-Halopropionic and β-Haloisobutyric Acids

| Formula of the ester | Boiling point (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ |  | Halogen contents (in %) |  | Literature data |  |  |  |
|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  | Calculated | Found | Calculated | Found | Boiling point (pressure in mm) | $d$ | $n_D$ | Reference |
| $ClCH_2CH_2COOC_4H_9$ | 92° (6)<br>89—91 (5) | 1.0370 | 1.4309 | 41.05 | 41.05 | 21.58 | 21.49 | 77—78° (6)<br>180 (160)<br>97—98 (8) | —<br>1.0728 (9°)<br>1.0368 (20) | 1.4312 (20°)<br>1.4389 (9)<br>1.4310 (20) | [1, 3, 4, 8] |
| $BrCH_2CH_2COOC_4H_9$ | 93—94 (13) | 1.3051 | 1.4549 | 43.98 | 43.62 | 38.25 | 38.30 | 130 (26) | 1.2773 (9) | 1.4577 (9) | [9] |
| $ICH_2CH_2COOC_4H_9$ | 104—105 (9) | 1.5232 | 1.4910 | 49.02 | 48.66 | 49.60 | 49.51 | — | — | — | — |
| $ClCH_2CH(CH_3)COOC_4H_9$ | 89—92 (10) | 1.0153 | 1.4310 | 45.66 | 45.51 | 19.89 | 19.78 | — | — | — | — |
| $BrCH_2CH(CH_3)COOC_4H_9$ | 95 (13) | 1.2508 | 1.4530 | 48.56 | 48.18 | 35.82 | 36.40 | 105 (20) | 1.2520 (8) | 1.4540 (8) | [2] |
| $ICH_2CH(CH_3)COOC_4H_9$ | 111—112 (4) | 1.4566 | 1.4850 | 53.60 | 53.11 | 47.02 | 46.87 | — | — | — | — |

TABLE 2

Saturation of Butyl Acrylate With Hydrogen Chloride (Molar Ratio of HCl to Butyl Acrylate 1 : 1)

| Amount $CH_2=CHCOOC_4H_9$ (in g) | Duration of saturation (in hours) | Yield of butyl ester of β-chloropropionic acid (in %) |
|---|---|---|
| 50 | 1.5 | 90.0 |
| 45 | 1.5 | 88.0 |
| 40 | 1.0 | 87.5 |
| 30 | 1.0 | 89.5 |
| 45 | 1.5 | 88.0 |
| 43 | 1.3 | 90.0 |
| 44 | 1.4 | 89.0 |
| 45 | 1.5 | 88.3 |

TABLE 3

Saturation of Butyl Methacrylate with Hydrogen Chloride (Molar Ratio of HCl to Butyl Methacrylate 1 : 1)

| Amount of $CH_2=C(CH_3)COOC_4H_9$ (in g) | Duration of saturation (in hours) | Yield of butyl ester of β-chloroisobutyric acid (in %) |
|---|---|---|
| 40.0 | 1.5 | 78.0 |
| 41.0 | 2.0 | 80.0 |
| 40.0 | 2.0 | 76.0 |
| 40.0 | 1.5 | 77.6 |

methacrylic acids were saturated with anhydrous hydrogen bromide; the esters were cooled (0°) and stirred mechanically during saturation. Hydrogen bromide was freed from traces of bromine (by absorption in a carbon tetrachloride solution of phenol) and dried over phosphorus pentoxide. It was introduced into the reaction bulb on the surface of the ester without being bubbled through the liquid layer. After achieving complete saturation (1 : 1 molar ratio) we kept the solution in a covered flask for 10-15 hours then fractionated at reduced pressure. Subsequently, the reaction mixture was washed with sodium sulfate and sodium carbonate solutions, then with water. Having dried the reaction mixture over anhydrous sodium sulfate, we fractionated it and collected the 93-94° (at 13 mm) fraction which contained butyl ester of β-bromopropionic acid; analysis corresponded to the indicated ester [9] (Table 1). The yield of this ester (based on the original ester) was 75-78%. We separated the 94-95° (at 13 mm) fraction [2] in the fractional distillation of the product obtained from the saturation of butyl ester of methacrylic acid. The yield of butyl ester of β-bromoisobutyric acid was 68-72%.

Synthesis of butyl ester of β-iodopropionic and β-iodoisobutyric acids. The method of preparing these is similar to the one described above. The absorption of anhydrous hydrogen iodide was carried out in a round-bottomed flask. Between the generator of hydrogen iodide and the reaction flask we interposed two U-tubes filled with red phosphorus and glass wool to trap any iodine vapor. The reaction product was kept in a covered flask for 10 hours at room temperature, and washed after that with solutions of sodium sulfite, sodium carbonate, and water. The reaction product was dried over anhydrous sodium sulfate and fractionally distilled; the 105° (at 9 mm) fraction was separated and corresponded (on the basis of composition) to butyl ester of β-iodopropionic acid (Table 1). From a distillation of wet butyl ester of β-iodoisobutyric acid we obtained a 55-58% yield of a 111-112° (at 4 mm) fraction which analyzed to the above-mentioned ester (Table 1).

## SUMMARY

1. We have synthesized and characterized butyl esters of β-chloro(bromo, iodo)-propionic and isobutyric acids.

2. The reaction in which anhydrous hydrogen chloride, bromide, and iodide add to butyl esters by acrylic and methacrylic acids was investigated.

## LITERATURE CITED

[1] Moureu, Murat, and Tampier, Ann. Chim. 15, 221, 239, 244 (1921).

[2] P. Bieber, Bull. Soc. Chim., 1950, 231, 291; 1951, 233, 655; 1952, 234, 1783; 1954, 199.

[3] V. N. Mikhailova and V. V. Pigulevskii, J. Appl. Chem., 30, 1843 (1957).*

[4] Brit. Pat. 654243 (1951).

[5] K. George, Science and Culture (India), 20, 46 (1954); Ch. A., 49, 3458 (1955).

[6] Moureu, Ann. Chim., (7), 2, 172 (1884).

[7] Ger. Pat. 53834 (1889).

[8] J. Kendall, Brit. J. Photogr., No. 4891, 82 (1954); Ref. J. Chem. 1955, 290, No. 8464.

[9] Moureu and Brown, Bull. Soc. Chim. (4), 27, 905 (1920).

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*Original Russian pagination. See C.B. translation.

# PREPARATION OF ω-HYDROXYPENTADECANOIC ACID BY THE METHOD OF ELECTROLYTIC CROSS-CONDENSATION. II

G. E. Svadkovskaia, E. K. Smol'ianinova, and V. N. Belov

In a preceding communication [1] we described the conditions for carrying out electrolytic condensation of ω-acetylhydroxyundecanoic acid with monoethyl adipate; these conditions enabled us to synthesize ω-hydroxypentadecanoic acid in a 25-27% yield (computed on the basis of original ω-acetylhydroxyundecanoic acid). Having at our disposal a considerably quantity of electrolysis products, we were able to conduct a detailed investigation of other compounds formed in this reaction.

As is well known, Kolbe synthesis is accompanied by a series of side reactions, the nature and quantity of which depend on the experimental conditions (current density, anode material, electrolyte concentration, temperature, pH of the medium, etc.) as well as on the structure of carboxylic acids undergoing electrolysis [2, 3]. In separate cases where Kolbe reaction was carried out, the following have been found to form: alcohols [4, 5], esters [6-8], carbonyl compounds [9-12], paraffin hydrocarbons [13, 14], and olefins [15, 16].

The subject of our investigation was a mixture of products obtained in a large scale electrocondensation of ω-acetylhydroxyundecanoic acid and monoethyl adipate under the following conditions: current density of the anode 25-30 amp/cm$^2$, molar ratio of ω-acetylhydroxyundecanoic acid to monoethyl adipate – 1 : 3, electrolyte dilution – 8.3 moles of $H_2O$ to 1 mole of reagent mixture, degree of neutralization – 0.875 moles of KOH per 1 mole of initial carboxylic acids; reaction was carried out at 50-65°.

As a result of our research, the following substances have been recovered from the investigated mixture: diethyl sebacate (II) (about 18%[*]), eicosanediol diacetate (III)[**] (about 10%), ethyl valerate (IV) (about 2%), ethyl pentenoate (V) (approximately the same quantity, 2%), decyl acetate (VI) 3-4%, decenyl acetate (VII) (3-4%), decanediol acetate (VIII) (about 0.5%), diethyl adipate (IX) (about 3%), monoethyl adipate (X) (the same quantity, 3%), free adipic acid (XI) (about 7%), and original ω-acetylhydroxyundecanoic acid (XII) (less then 1%); the main reaction product – ethyl ω-acetylhydroxypentadecylate (I), made up 16% of all the electrolysis reaction products.

Formation of these compounds in the investigated reaction could be explained on the basis of existing ideas about the course of similar electrolytic processes [2]. The formation of compounds (I) – (VIII), for example, could be represented in the following manner:

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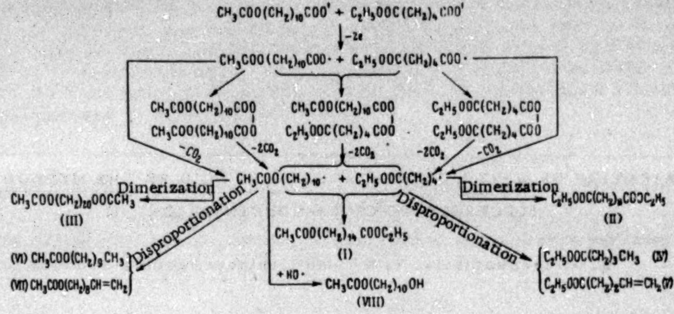
[*] This and the succeeding numbers give yield as % of the over-all quantity of products isolated after electrolysis.

[**] The conditions under which the reaction mixture was treated (preliminary saponification) enabled us to isolate this diol as well as decanediol in a free state. However, analytical data (OH group determination) makes us believe that these diols exist as di- and monoacetates, respectively, in the reaction mixture.

Reaction Scheme of the Electrolytic Condensation of ω-Acetylhydroxyundecanoic Acid With Monoethyl Adipate


CH₃COO(CH₂)₁₀COO' + C₂H₅OOC(CH₂)₄COO'
-2e
CH₃COO(CH₂)₁₀COO· + C₂H₅OOC(CH₂)₄COO·
-CO₂
-2CO₂
-CO₂
Dimerization
Disproportionation
CH₃COO(CH₂)₁₀· + C₂H₅OOC(CH₂)₄·
CH₃COO(CH₂)₂₀OOCCH₃
(III)
C₂H₅OOC(CH₂)₈COOC₂H₅
(II)
CH₃COO(CH₂)₁₄COOC₂H₅
(I)
(VI) CH₃COO(CH₂)₉CH₃
(VII) CH₃COO(CH₂)₈CH=CH₂
C₂H₅OOC(CH₂)₃CH₃ (IV)
C₂H₅OOC(CH₂)₂CH=CH₂ (V)
+HO·
CH₃COO(CH₂)₁₀OH
(VIII)

Diethyl adipate (IX) and free adipic acid (XI) could have been formed by trans-esterification of the original monoethyl esters.

## EXPERIMENTAL

The reaction mixture obtained in the electrolysis[*] separated into two immiscible layers; the upper oily layer contained neutral electrocondensation products, while the lower aqueous alkaline solution consisted of acidic substances in the form of salts. The ratio of the neutral substances to the alkaline solution was approximately 1 : 2.2 by weight.

I. Investigation of neutral substances. In all we have separated and subjected to investigation about 6 kg of a mixture consisting of neutral products. Preliminary separation was achieved through steam-distillation of highly volatile components and rough fractional vacuum-distillation of substances nonvolatile with steam. In one such separation, out of an 800 g sample (previously washed thoroughly with water till washings showed a neutral reaction) we steam-distilled 94.5 g (i.e. about 12%) of highly volatile substances. From the fractional distillation of the remainder we collected the following fractions: 1st, 96-155° (at 7 mm), 108.8 g (13.6% of all neutral products); 2nd, 155-180° (at 7 mm), 195 g (24.4%); 3rd, 180-230° (at 7 mm), 180.8 g (22.6%); plus 139 g (17.4%) of residue.

Later on in our investigation, we combined all the corresponding fractions obtained from different portions of the neutral mixture.

a) Substances volatile with steam. As a result of repeated fractionations at atmospheric pressure, 700 g of substances volatile with steam were separated into two main fractions: 1st, 142-155° (s.v.[**] 407.2, br.n. 68.9), 280 g (40% by weight of substances fractionated); 2nd, 230-250° (s.v. 305.7, MR.n. 3.2, br.n. 35.4), 259 g (~ 37%).

The 142-155° fraction was saponified with alcoholic potassium hydroxide; 270 g of it was heated over a water bath with 1550 ml of 12% alcoholic potassium hydroxide for 1 hour, and 30 minutes more after adding to it 300 ml of benzene. After the proper treatment we isolated an insignificant quantity (2.8 g) of neutral substances (b.p. 105-170°, br.n. 62.2% OH 11.7[***]) and 172 g of acidic substances, which when fractionated gave in turn three new fractions.

1st, 180-185° (RM.n. 551.3, br.n. 82.7), 61 g; 2nd, 185-189° (RM.n. 551.4, br.n. 84), 78 g; 3rd, 189-195° (RM.n. 541.9, br.n. 85.6), 18.2 g.

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[*] The conditions for electrocondensation were given in the introductory section.

[**] Here and further on, s.v. = saponification value, RM.n. = Reichert-Meissel number, br.n. = bromine number.

[***] In all the cases the OH contents of neutral products was determined by acetylation at room temperature.

According to literature data, valeric acid has a b.p. 185.35° [17], pentene-4-oic acid,a b.p. 188-189° [18]. Calculated RM.n. 549 for $C_4H_9COOH$ and for $C_4H_7COOH$, RM.n. 560, br.n. 160.

These data indicate that each of the obtained fractions is a mixture of valeric and pentenoic acids in approximately equal amounts. In view of the fact that it was not practically feasible to separate these acids by fractionation, we hydrogenated the fractions catalytically (Raney Ni as catalyst, 100 atm. pressure, 50° temperature). All three fractions gave valeric acid on hydrogenation.

B. p. 185-187°, RM.n. 545.5, $d^{20}_4$ 0.9387, $n^{20}D$ 1.4118, $MR_D$ 27.05; calc. 26.83; anilide, m.p. 62-62.5°. According to literature data for pentanoic acid [17], $d^{20}_4$ 0.9387; anilide, m.p. 63°.

Found %: N 7.67, 7.94; $C_{11}H_{15}ON$. Calculated %: N 7.91.

The 230-250° fraction was saponified similarly; 250 g of the fraction gave 132 g of neutral substances and 42 g of acids. A crystalline component of the latter ones was isolated (18.5). The crystalline acid was recrystallized from hot water and had m.p. 149-150°, RM.n. 762. Adipic acid is listed with m.p. 149-150° [19], calculated RM.n. 767. A sample mixed with known adipic acid gave no melting point depression. The liquid part of the acids (about 23 g) distilling over at 74-140° (at 4 mm), RM.n. 326.6, br.n. 52.6, was evidently a mixture of saturated and unsaturated monobasic acids.

Almost all the neutral substances (132 g) distilled over in the 224-230° range and turned out to be a mixture of decyl and decylene alcohols in approximately equal amounts.

Found %: OH 10.48. Br.n. 54.6. $C_{10}H_{21}OH$. Calculated %: OH 10.76. $C_{10}H_{19}OH$. Calculated %: OH 10.89. Br.n. 102.5.

We obtained 93 g of decyl alcohol by hydrogenating 100 g of this mixture (Raney Ni, 100 atm., 50°).

B. p. 227-230°, $d^{20}_4$ 0.82965, $n^{20}D$ 1.4373, $MR_D$ 49.93; calc. 49.9. Literature data [20]: b.p. 228-232°, $d^{20}_4$ 0.8297, $n^{20}D$ 1.43719.

3,5-Dinitrobenzoate of this alcohol had a m.p. 56-57°. A sample of it mixed with a derivative of known decyl alcohol had the same melting point. Literature data gives [21] m.p. 57°.

Found %: N 8.17, 8.21. $C_{17}H_{24}O_6N_2$. Calculated %: N 7.95.

b) The 96-155° (at 7 mm) fraction. From 200 g of this fraction (RM.n. 5.2, s.v. 396.5, br.n. 23.4, % OH 0.3) we separated (after a two-fold fractional vacuum-distillation) a 112.5 g mixture of products distilling over at 105-122° (at 7 mm). It was investigated in the way previously described for substances volatile with steam and was shown to contain an adipate plus a mixture of decyl and decenyl acetates. Their saponification products, adipic acid (26 g) and a mixture of the above-mentioned alcohols (41 g), were identified in a way previously described.

c) The 155-180° (at 7 mm) fraction. We fractionally distilled 190 g of this fraction (RM.n. 2.0, s.v. 377.3, br.n. 0.18, % OH 0.2) and collected 160 g of a product in the range 132-180° (at 7 mm) which, after saponification and appropriate treatment, gave 15.8 g of neutral substances and 87 g of sebacic acid, m.p. 134-134.5°, RM.n. 549.8 (calculated RM.n. 554 for sebacic acid, listed m.p. 134.5° [22]). A mixed sample with known sebacic acid melted at the same temperature.

Fractional crystallization of the neutral products gave 2.9 g of 1,10-decanediol, m.p. 71-72° (from benzene).

Listed m.p. 70.8-71.8° for this decanediol [23].

Found %: C 68.79, 69.02; H 12.96; 12.68; OH 19.4. $C_{10}H_{22}O_2$. Calculated %: C 68.91; H 12.72; OH 19.5.

d) The 180-230° (at 7 mm) fraction. We saponified and processed [1] 180 g of this fraction (RM.n. 324.8, br.n. 2.6, % OH 0.34) collecting 115.8 g of $\omega$-hydroxypentadecanoic acid. Recrystallization from benzene gave 91 g of this acid, m.p. 85-85.5° (according to literature data [24]: m.p. 84.8-85.2°).

Found %: C 69.96, 70.07; H 11.79, 11.86; OH 6.61. RM.n. 217.7. $C_{15}H_{30}O_3$. Calculated %: C 69.72; H 11.70; OH 6.59. RM.n. 217.

Besides this, we isolated 21.6 g of 1,20-eicosanediol. This one had a m.p. 102-103° after recrystallization from benzene (according to literature data [25]: m.p. 103°).

Found %: C 76.28, 76.80; H 13.66, 13.58; OH 10.3. $C_{20}H_{42}O_2$. Calculated %: C 76.36; H 13.46; OH 10.8.

e) Residue from fractional distillation. Vacuum distillation of neutral electrolysis products left 132 g of residue; after saponification with alkaline KOH and appropriate treatment, we isolated 48 g of 1,20-eicosanediol, m.p. 102-103° (it gave no melting point depression when mixed with the diol obtained from the 180-230° (at 7 mm) fraction), 72 g of acidic substances containing ω-hydroxypentadecanoic acid. By esterifying the acid mixture with ethyl alcohol we obtained a 56 g mixture of esters which was fractionally distilled in vacuum (at 0.01-0.04 mm) to give 7.8 g of ethyl ω-hydroxypentadecylate, m.p. 48.5-49° (from methanol, then from petroleum ether).

Found %: C 71.70, 71.60, H 11.82, 11.82, OH 6.1. s.v. 197.9. $C_{17}H_{34}O_3$. Calculated %: C 71.28; H 11.96; OH 5.9. s.v. 195.8.

II. Investigation of acidic substances isolated from aqueous alkaline solution. The data below refer to the products isolated from 3 kg of aqueous alkaline solution. Admixtures of neutral substances were extracted with benzene, while acidic ones were salted out of solution by acidification with hydrochloric acid (to a congo red end-point). The precipitate of adipic acid was separated by filtration (76 g,* m.p. 149-150°, RM.n. 759.8; did not give melting point depression when mixed with known adipic acid), whereas the mixture of liquid acids was separated and dissolved in ether. After evaporation of the solvent (the solution underwent preliminary washing with water until washings gave a neutral test) we obtained a 111.3 g mixture of acids; when fractionated in vacuum, these gave two main fractions: 131-134° (at 3 mm), 42.2 g, and 180-220° (at 3 mm), 39.2 g.

The 131-134° (at 3 mm) fraction, RM.n. 320.0, s.v. 321.9 turned out to be monoethyl adipate, for which the calculated RM.n. and s.v. were 322.0. When 40 g of this ester was saponified it gave 28.6 g of adipic acid, m.p. 149.5-150°, RM.n. 759.8; a mixed sample with known adipic acid gave no melting point depression.

Processing of the 180-220° (at 3 mm) fraction with a small quantity of ether yielded 13.8 g of adipic acid (m.p. 149-150°, RM.n. 758.3; mixed sample with known acid gave no melting point depression). Another 2.7 g of adipic acid were isolated from the ether solution by fractional crystallization after evaporating the solvent. The remaining liquid acids (22 g) were distilled in vacuum, and the main fraction was 185-190° (at 3 mm), RM.n. 275.8, s.v. 218.3, weight 11.3 g. After being washed with hot water (to free it from any admixture of adipic acid) this fraction had a RM.n. 229.3 and s.v. 243.7. (For ω-acetylhydroxyundecanoic acid these are given [24], b.p. 185° at 2 mm, calculated RM.n. and s.v. 230). When this acid – ester was saponified, it yielded 6.4 g of ω-hydroxyundecanoic acid, m.p. 68.5-69.5° (according to literature data [24]: m.p. 70-70.5°); a mixed sample with known ω-hydroxyundecanoic acid did not give a melting point depression.

Found %: OH 8.1, RM.n. 281. $C_{11}H_{22}O_3$. Calculated %: OH 8.4. RM.n. 277.

## SUMMARY

1. We have thoroughly studied the mixture of products obtained from an electrolytic cross-condensation between ω-acetylhydroxyundecanoic acid and monoethyl adipate in a Kolbe reaction. It was established that the above-mentioned mixture contained ethyl ω-acetylhydroxypentadecylate (~ 16%), diethyl sebacate (~ 18%), eicosanediol diacetate (~ 10%), ethyl valerate (~ 2%), ethyl pentenoate (~ 2%), decyl acetate (3-4%), decenyl acetate (3-4%), decanediol acetate (less than 1%), diethyl adipate (~ 3%), adipic acid (~ 7%), monoethyl adipate (~ 3%), and ω-acetylhydroxyundecanoic acid (less than 1%).

2. We have shown that the formation of the compounds isolated could be explained on the basis of commonly accepted ideas about the mechanism of Kolbe reaction.

## LITERATURE CITED

[1] G. E. Svadkovskaia, S. A. Voitkevich, E. K. Smol'ianinova, V. N. Belov, J. Gen. Chem., 27, 2146 (1957).**

---

* Another 8.3 g of adipic acid was obtained when the aqueous solution was evaporated.

**Original Russian pagination. See C.B. translation.

[2] B. C. L. Weedon, Quart. Revs., 6, 380 (1952).

[3] F. Fichter, Organische Electrochemie, Dresden and Leipzig (1942).

[4] Kunugi Taiseki, J. Am. Chem. Soc., 75, 1597 (1953).

[5] F. Fichter and M. Rudin, Helv. Chim. Acta, 24, 398 (1941).

[6] J. Hamonet, C. r. 123, 252 (1896).

[7] J. Petersen, Z. phys. Ch., 33, 99 (1900).

[8] S. Goldschmidt, W. Leicher and H. Haas, Lieb. Ann., 577, 153 (1952).

[9] J. Petersen, Z. phys. Ch., 33, 295 (1900).

[10] F. Fichter, A. Bürgin, Helv. Chim. Acta, 14, 90 (1931).

[11] F. Fichter and O. Leupin, Helv. chim. Acta , 21, 616 (1938).

[12] F. Fichter and A.Petrovitch, Helv. chim. Acta, 23, 806 (1940).

[13] J. Petersen, Z. Elektroch., 20, 328 (1914).

[14] W. Schanzer, K. Clusius, Z. phys. Ch. 190, A 241 (1942).

[15] P. Hölemann and K. Clusius, Ber., 70, 819 (1937).

[16] K. Hopfgartner, Helv. chim. Acta, 32, 523 (1911).

[17] Dictionary of Org. Compds. 3, 909 (1949).*

[18] Dictionary of Org. Compds. 1, 47 (1949).*

[19] Dictionary of Org. Compds. 1, 31 (1949).*

[20] Dictionary of Org. Compds. 1, 617 (1949).*

[21] R. Shriner and R. Fuson, Systematic Identification of Organic Compounds II., 223 (1950) [Russ. trans.].

[22] Dictionary of Org. Compds. 3, 623 (1949).*

[23] K. Folkers and H. Adkins, J. Am. Chem. Soc., 54, 1145 (1932).

[24] P. Chuit and J. Hausser, Helv. Chim. Acta, 12, 463 (1929).

[25] P. Chuit and J. Hausser, Helv. Chim. Acta, 12, 850 (1929).

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*In Russian.

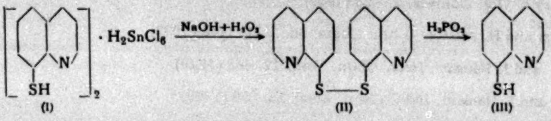
# A SIMPLIFIED SYNTHESIS OF 8-MERCAPTOQUINOLINE (THIOOXINE) AND PREPARATION OF ITS POTASSIUM AND SODIUM SALTS

Iu. A. Bankovskii, A. F. Ievin'sh, and E. A. Luksha

8-Mercaptoquinoline (thiooxine) was synthesized for the first time by A. Edinger [1]. As our studies have shown, it turned out to be a very valuable reagent in qualitative and quantitative determinations of small amounts of palladium, copper, molybdenum, rhenium, manganese, and other elements.

One of us had previously [2] redefined more accurately the conditions for carrying out the separate stages of thiooxine synthesis proposed by Edinger. The preparation of benzoyl derivative of thiooxine was the most capricious step in this synthesis. Even in a large experiment this step would occasionally proceed in an unsatisfactory manner.

We discovered that the step in which benzoyl derivative of thiooxine was prepared could be eliminated. To do this, we oxidized the sodium salt of thiooxine (formed when alkali reacted with chlorostannate salt of (I)) with hydrogen peroxide to a disulfide (II) which formed an insoluble precipitate in alkaline solutions. The disulfide could easily be purified and reduced to thiooxine (III). We have tried a series of reducing agents used to reduce disulfides to mercaptans; sodium and potassium sulfides [3, 4], glucose [5, 6] sodium sulfite, potassium metabisulfite, and others. Meanwhile we found out that the most active and convenient reducing agent for our case was hypophosphorous acid (we used potassium hypophosphite in hydrochloric acid). The reduction of thiooxine disulfide into thiooxine proceeded quantitatively without any side reactions.



A method of reducing inorganic sulfates to hydrogen sulfide has been described in the literature [7] (a quantitative method for the determination of sulfates with hypophosphorous acid in the presence of hydriodic acid). Attempts to reduce quinoline-8-sulfonic acid (first of the products in Edinger's thiooxine synthesis) directly to 8-mercaptoquinoline (thiooxine), using this method, did not give positive results; no traces of 8-mercaptoquinoline were detected. But for thiooxine disulfide, hypophosphorous acid alone (even in the absence of hydriodic acid) was an excellent reducing agent.

Thiooxine was formed during neutralization of hydrochloric acid and precipitated in the form of bright-red $C_9H_6NSH \cdot 2H_2O$ crystals. It was very difficult to obtain this crystal dihydrate of thiooxine in a dry form by simply drying the precipitate in air (it gradually oxidized). When dried over even very weak drying agents, it lost all the water of crystallization and changed into anhydrous thiooxine, a thick blue or blue-violet liquid. Water of crystallization was also easily lost in vacuum (without drying agents). Therefore, the best way to obtain the crystal dihydrate of thiooxine was to dry it for 10-12 hours in a vacuum-dessicator at room temperature till it changed into anhydrous liquid, and then to keep it in a well-evacuated desiccator the bottom of which was filled with water. Under these conditions, in about 2-3 hours, anhydrous thiooxine was converted into beautiful dark-red hydrate crystals. The compound was not very stable in this state. It gradually oxidized to disulfide (50% of the crystal hydrate compound was oxidized when kept in a covered vessel for a year). Thiooxine salts were considerably more stable. The hydrochloride (previously described by us) could be stored for many years in covered vessels, but it was very easily hydrolyzed by water vapor forming thiooxine crystal hydrate which then gradually oxidized in air.

In view of the fact that thiooxine is a much stronger acid than oxine, it forms much less hydrolyzable salts with alkali metals. Consequently, potassium and sodium salts of thiooxine are more difficult to oxidize than hydrochloride and permit a prolonged storage of the compound.

Reduction of disulfide to thiooxine and preparation of its sodium and potassium salts is described below.

## EXPERIMENTAL

Preparation of quinoline-8-sulfonic acid. As our experiments have shown (confirmed also by literature data [8]), quinoline was sulfonated best with very strong fuming sulfuric acid containing 50-55% of free $SO_3$. Moreover, it turned out to be more convenient to first convert the quinoline into its sulfate (using a calculated amount of concentrated sulfuric acid) which was then gradually added in small portions to a 4-fold excess of 60-65% fuming sulfuric acid. At the same time, the concentration of fuming sulfuric acid decreased to 50%. The mixture was kept at 160° for 3 hours. When undistilled (common reagent grade) quinoline was used, the yield of quinoline--8-sulfonic acid was 62-65%. When carefully fractionally distilled quinoline was used, the yield of sulfonic acid was 80% [8].

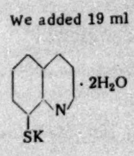
Preparation of quinoline-8-sulfonyl chloride and its reduction to a chlorostannate salt (I) was previously described [2].

Preparation of thiooxine disulfide (II). We carefully washed 100 g of wet chlorostannate salt (I) on a suction filter and added to it a solution containing 50 g of NaOH in the least possible amount of water; addition was carried out in small portions with stirring until a homogeneous paste was formed. This paste was diluted with 0.5 liter of water and filtered. If an appreciable amount of sodium salt remained on the filter, it was taken off and dissolved in a small quantity of hot water then filtered once more. The filtrates were combined. If the filter retained a considerable quantity of undissolved yellow salt, then the treatment with alkali was repeated (as described above) using a correspondingly smaller quantity of NaOH solution. We cooled the turbid dark-yellow filtrate in an ice bath and added to it (until discoloration) 40 ml of 30% hydrogen peroxide with stirring. This was accompanied by precipitation of white, amorphous-appearing thiooxine disulfide, which was filtered out with suction, washed 2-3 times with 2% NaOH solution and few times with water, then dried at 120°. We obtained 18-18.5 g of disulfide.

Reduction of thiooxine disulfide. We dissolved 18 g of disulfide in 360 ml of concentrated hydrochloric acid and added 24.3 g of potassium hypophosphite. After half an hour of mild refluxing the reaction mixture was cooled, and crystals of KCl were filtered out. The filtrate was transferred into a 2-liter beaker and carefully neutralized (with rapid stirring) with saturated sodium carbonate solution (140 g of anhydrous sodium carbonate in 320 ml of twice-distilled water) to a pH 5.5-6. Towards the end point we frequently checked the pH of the medium (with paper universal indicator), since at a pH above or below 5.5-6 thiooxine would dissolve, thus decreasing the yield of the product. The bright-red crystalline precipitate of thiooxine dihydrate was filtered with suction, washed on the filter with three 50 ml portions of twice-distilled water, and pressed out (on the filter) as thoroughly as possible. We obtained 25 g of wet thiooxine dihydrate.

It is important to note, that all the reagents used in the reduction of disulfide to thiooxine must be of a high degree of purity (AR grade), since any heavy metals present in the reagents will be completely retained in thiooxine. The presence of iron and traces of copper are particularly intolerable.

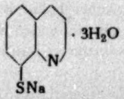
Preparation of potassium salt of thiooxine. We added 19 ml of 50% KOH (AR grade) to 25 g of dry, well



pressed-out thiooxine, stirring the mixture carefully. The mixture turned lemon-yellow. It was heated until everything dissolved, then cooled. We added 1.5-2 ml of isoamyl alcohol and mixed till a homogeneous consistency was achieved. We filtered it with suction and washed the yellow potassium salt with one portion of isoamyl alcohol (10 ml). The isoamyl alcohol was thoroughly sucked away and the salt washed 3 times with ether (50 ml portions). To purify 13 g of thoroughly pressed-out (on the filter) wet potassium salt, we mixed it with 70 ml of ethyl alcohol (redistilled) and heated to boil. The hot solution was filtered with suction through a double filter and cooled. We added to it 400 ml of ether and after a few minutes filtered out the precipitated crystals of potassium thiooxine salt which were washed on the filter paper with two portions of ether (30 ml each). We obtained 10-12 g of potassium thiooxine salt, which constituted 20-24% of the quinoline used.

Found %: H 4.21; S 13.48; N 5.84. $C_9H_6NSK \cdot 2H_2O$. Calculated %: H 4.24; S 13.60; N 5.95.

Preparation of sodium salt of thiooxine. We added 60 ml of 16.5% NaOH solution to 25 g of thoroughly pressed out (on a suction filter) thiooxine dihydrate, carefully stirred the mixture till a lemon-yellow homogeneous mass was formed; we filtered it with suction



pressed out (on a suction filter) thiooxine dihydrate, carefully stirred the mixture till a lemon-yellow homogeneous mass was formed; we filtered it with suction, washed with 10 ml of isoamyl alcohol, and then with three 20 ml portions of ether. We obtained 21 g of sodium salt. To purify this salt, we dissolved it in 290 ml of boiling alcohol and filtered. After the filtrate cooled completely, we added to it 300 ml of ether and after a few minutes filtered out the yellow crystals which were then washed on a suction filter with 20 ml of ether. We obtained 13 g of pure sodium salt of thiooxine.

Found %: H 4.85; S 13.33; N 5.75. $C_9H_6NSNa \cdot 3H_2O$. Calculated %: H 5.07; S 13.50; N 5.91.

Sodium and potassium salts gave a transparent yellow or slightly reddish solution when dissolved in water; after being stored in air, they formed a light suspension of disulfide. Dry compounds were stable for a long time if stored in covered containers. Aqueous solutions of potassium and sodium salts of thiooxine were not very stable and would oxidize to disulfide in two or three weeks. For analytical purposes a 5% solution of thiooxine salts in 2.5-6 N hydrochloric acid is usually used; these are stable for a few weeks (in 2.5 N HCl) or months (in 6 N HCl).

## SUMMARY

1. The course of thiooxine synthesis was altered after the reduction of quinoline-8-sulfonyl chloride with stannic chloride; chlorostannate salt was decomposed with alkali, oxidized with hydrogen peroxide to disulfide, which was then reduced with potassium hypophosphite in hydrochloric acid solution.

2. We prepared a potassium salt of thiooxine stable in storage. We also established the composition of potassium and previously obtained sodium salt of thiooxine.

## LITERATURE CITED

[1] A. Edinger, Ber., 41, 938 (1908).

[2] J. Bankovski, Latvijas PSR Zinātnu Akademijas Vēstis, 1952, 12, 127.

[3] T. S. Price and D. F. Twiss, J. Chem. Soc., 91, 2021 (1907).

[4] K. Brand, Ber., 42, 3464 (1909).

[5] H. Lecher and K. Simon, Ber., 55, 2427 (1922).

[6] G. M. Badger and R. G. Buttery, J. Chem. Soc., 1956, 3237.

[7] E. E. Archer, Analyst, 81, 181 (1956).

[8] A. Inove, M. Sugiura and J. Tsuzuki, Bull. Chem. Soc., Japan, 27, 430 (1954).

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# CONVERSION OF $\Delta^3$-p-MENTHENE ON GUMBRINE*

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Research in the field of cyclic hydrocarbon isomerization on natural aluminum silicate catalysts is closely connected with the problem of origin and transformations of petroleum. Isomerization of aromatic and certain naphthene (alicyclic) hydrocarbons has been comparatively well-investigated, while in that respect other cyclic hydrocarbons with one or two double bonds in the ring have hardly been studied at all. This paper should partially fill in this gap.

We did not find any papers in the literature on the isomerization of menthene on natural aluminum silicate catalysts. N. D. Zelinskii and G. S. Pavlov [1] have studied isomerization of menthene and obtained menthane and cymene after passing menthene vapors over platinized asbestos in a stream of carbon dioxide. In this respect cyclohexene has been studied much more fully [2-5] (methene is its derivative). Works on the isomerization of cyclohexene on aluminum silicate catalysts were done in the range of 320-450°, but according to the theory of isoastazy the maximum possible temperature to which petroleum could have been subjected in its formative process could not be considered higher than 250°. For this reason (in this work) our experiments on isomerization of $\Delta^3$-p-menthene were done at 170-230°.

## EXPERIMENTAL

$\Delta^3$-p-Menthene used in the experiments was prepared by dehydration of menthol over activated alumina at 320°, in a high pressure autoclave; the method was worked out by V. N. Ipatiev [6] for the dehydration of 1-methylcyclohexanol-2. The menthol used melted at 45° and boiled in the 197-210° range. The synthesized $\Delta^3$-p-menthene had the following properties: b.p. 166-169°, $d^{20}_4$ 0.8114, $n^{20}D$ 1.4515. Its nitrosochloride melted at 112°; according to Chugaev's data, nitrosochloride of $\Delta^3$-p-menthene had a m.p. 113° [7].

As a catalyst for the menthene isomerization we used gumbine activated with hydrochloric acid and with a specific surface of 142.3 $m^2/g$. at a pH 2.32. We found the optimum isomerization conditions by running a series of experiments at various temperatures with different amounts of catalyst, and lengths of heating time. These turned out to be 10 hours heating at 195° with 10% catalyst.

The menthene in these experiments was sealed off in thick-walled glass ampules which were then heated in an autoclave to avoid any loss of compound in case of cracking. When the ampules were opened after heating, no pressure was observed inside. Heating of menthene was accompanied by appreciable polymerization (the yield of polymers could attain 34-35% of inclosed compound). The catalysis product from a few experiments had the following properties: b.p. 90-170°, $d^{20}_4$ 0.8065 and $n^{20}D$ 1.4459. It was subdivided into 11 fractions in a distillation column with 20 theoretical plates (total reflux value −20).

The fractions boiling in the ranges 150-158° (1.22 g), 158-160° (0.82 g), and 160-161° (0.55 g) had very similar refractive indices (1.4382, 1.4383, and 1.4386 respectively). These fractions were combined and treated with 98% sulfuric acid to remove aromatic hydrocarbons (their presence was determined in each fraction by the formolytic reaction**). After removal of tars, washing and drying, the remaining part boiled at 161-162°, and had $d^{20}_4$ 0.7881 and $n^{20}D$ 1.4329. These constants agreed well with those of 1,2-dimethyl-3-isopropylcyclopentane.

From the succeeding five fractions boiling in the 162-171° interval we separated some narrower ones: 165.5-166.5°, 166.5-167.5°, 167.5-168.5°, and 168.5-169.2°. In these fractions we have also established the presence of aromatic hydrocarbons using the formolytic reaction. After treatment with sulfuric acid (d 1.69), to remove terpenes, we determined the aromatic hydrocarbon contents of these fractions (11.76, 13.10, 14.14, and 17.47% respectively) by the aniline method. Treatment with sulfuric acid removed aromatic hydrocarbons, and the refractive indices of individual fractions turned out to be almost identical ($n^{20}_{D}$ 1.4382 to 1.4392). and were close to that of p-menthane ($n^{20}_{D}$ 1.4393). The densities ($d^{20}_{4}$ from 0.7952 to 0.7981) were also close to that of p-menthane.

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*(Tr. Note): a fuller's earth from Kutais, Georgia (Transcaucasia).

**(Tr. Note): a test with $AlCl_3$ and $CHCl_3$.

In order to ascertain whether these fractions contained cyclopentane derivatives, we combined and subjected them to catalytic dehydrogenation over Zelinskii's nickel-aluminum catalyst; the mixture was passed at the rate of 8 drops a minute. After sixth passage over the catalyst, the refractive index of the original mixture increased from 1.4389 to 1.4640 and did not change any further. The product of dehydrogenation had a b.p. 166-172°, $n^{20}_{D}$ 1.4640, $d^{20}_{4}$ 0.8281 and aniline point − 4°; after treatment with 98% sulfuric acid it boiled at 162-163°, and had $n^{20}_{D}$ 1.4335, $d^{20}_{4}$ 0.7892, and aniline point + 58°. These constants were in good agreement with those of 1,2-dimethyl-3-isopropylcyclopentane. We tried unsuccessfully to isolate aromatic hydrocarbons.

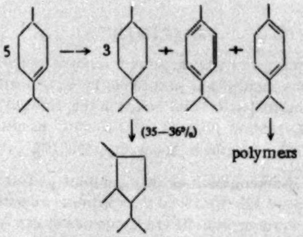
A quantitative composition tabulation of fractions in the 165.5-169.2° range showed that they contained 58.1% cyclohexene, 21.0% cyclopentane, 21.7% aromatic, and 0.2% terpene hydrocarbons. The quantity of cyclopentanes was 35-36% the amount of cyclohexanes; the same ratio of these hydrocarbons was observed in the isomerization of cyclohexane on gumbrine [8].

The polymers ($d^{20}_{4}$ 0.9342) were distilled in vacuo. The bulk of the material distilled in the 290-310° (at 3 mm) range.

Found %: C 88.09; H 11.82. M 282.

These data showed that the polymers were basically composed of terpinene dimers.

The results presented above permit the assumption of the following scheme for the isomerization of $\Delta^3$-p-menthene on gumbrine.



## SUMMARY

The conversion of $\Delta^3$-p-menthene on gumbrine was studied. We showed that isomerization of $\Delta^3$-p-menthene was accompanied by redistribution of hydrogens and ring contraction. As a result of isomerization, a complex mixture of hydrocarbons was formed out of which we isolated 1,2-dimethyl-3-isopropylcyclopentane, and p-menthane. About 34-35% of $\Delta^3$-p-menthene polymerized during isomerization. The polymers were terpinene dimers.

## LITERATURE CITED

[1] N. Zelinski and G. Pavlov, Ber., 57, 1066 (1924).

[2] N. D. Zelinskii, and Iu. A. Arbuzov, Proc. Acad. Sci. USSR, 24, 793 (1939).

[3] N. D. Zelinskii, Proc. Org. Chem. Session, Acad. Sci. USSR, 8 (1939).

[4] A. F. Nikolaieva, V. M. Tatevskii and A. V. Frost, J. Gen. Chem. 15, 796 (1945).

[5] F. Iu. Rachinskii and N. I. Rzhekhina, J. Gen. Chem. 5, 601 (1955).*

---

*Original Russian pagination. See C.B. translation.

[6] N. V. Ipat'ev and O. Rutala, J. Russ. Chem. Soc. 44, 1692 (1912).

[7] L. A. Chugaev, J. Russ. Chem. Soc. 35, 1116 (1903).

[8] V. V. Tishchenko and N. V. Petrova, Sci. Rep. Leningrad State University, Chem. Sci. Series, No. 15, 147 (1957).

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# A STUDY OF GLUCOSIDES OF JUTE

## I. OLITORISIDE

N. K. Abubakirov, V. A. Maslennikova and M. B. Gorovits

Although the first news about the poisonous principles of jute date to the end of the past century [1], the most dependable data were secured only much later by Sen [2]. He established the presence in the seeds of Corchorus capsularis L. of a glucoside, corchorine, which contains an unsaturated lactone group and which belongs to the cardiac glucosides of the digitalis group. By hydrolysis of corchorine with sulfuric acid, Sen obtained a molecule of glucose and a crystalline aglucone, corchogenine. Soliman and Saleh [3], found, contrary to Sen, that corchorine does not suffer any changes in acid hydrolysis and that for this reason it is an aglucone while the substance which had been named corchorine is nothing else but strophantidine. Ahmed and co-workers [4, 5] dispute the opinion about the identity of corchorine and strophantidine and cite experimental material which supports Sen's work. Some other papers [6-12] have been also devoted to the study of jute glucosides from C. capsularis as well as of C. olitorius. In the last of these papers Frerejacque and Durgeat [12] describe, specifically, corchorazide A which includes strophantidine as the aglucone portion, which fact agrees to some degree with the work of Soliman and Saleh.

We examined the seeds of the long-fruited jute (Corchorus olitorius L.) which has been developed widely in in recent years in the republics of Central Asia (variety No. 420). A tincture of the seeds in 70% alcohol had a rather high cardiotonic acitivity, which was equal to 500 frog units of activity per gram of the seeds. The method of isolation of the glucosides is presented in the experimental part. Special attention was paid to insure that all operations, including even the distillation of the solvents, be run at temperatures not above 40-45°. The action of alkaline or acidic reagents was also excluded. Specifically, in contrast to other investigators [2, 3, 5, 8, 9] we refused to precipitate the excess lead ions with hydrogen sulfide. The latter circumstance is not unimportant since according to our observations the jute glucosides are easily hydrolyzed under conditions of even a weakly acidic medium.

The substance isolated by us gave all the tests characteristic of cardiac glucosides of the group of digitalis-strophanthum. The elemental analysis of the product, combined with the molecular weight determined by alkalimetric titration method, leads to the formula $C_{35}H_{52}O_{14}$. No methoxy groups were found. The ultraviolet absorption spectrum is characterized by the presence of two maxima at 218-304 mμ (Fig. 1). The presence of a large number of oxygen atoms permits the substance to be placed among diglucosides. In its physicochemical properties the substance obtained by us differs noticeably from other known glucosides and for this reason the new glucoside was named olitoriside. Olitoriside is one of the most toxic cardiac glucosides: in 1.0 g of the biocide there are 11,000 cat or, respectively, 64,000 frog units of activity.*

The ease with which the hydrolytic cleavage of the glucoside occurs indicates that the nearest sugar to the genine in olitoriside must be a 2-desoxy sugar. The crystalline genine, formed in the hydrolysis, has the elemental composition $C_{23}H_{32}O_6 \cdot {}^1/_2\, H_2O$, m.p. 178° and $[\alpha]^{25}D + 40.3°$ (c 2.6; methanol). The ultraviolet absorption spectrum shows two characteristic maxima at 217 and 303 mμ (see Fig. 1). All these data agree well with the properties of the known cardiac aglucone, strophanthidin. The mixed melting point with an authentic sample of strophanthidin gave no depression. However, since the original argument in the literature, as indicated above, developed around the question whether or not corchorine is the specific jute glucoside or whether ordinary strophanthidin had been described as a distinct substance under the name of corchorine, we also prepared some of the derivatives of the aglucone. All these in their properties turned out to be identical with the analogous derivatives of strophanthidin. Finally, we measured the infrared absorption spectra of both compounds (Fig. 2) which confirmed their total identity.

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* The pharmacological study of olitoriside was done at the All-Union Institute for Medicinal and Aromatic Plants by A. D. Turova.

Thus, the material secured by us makes us join those authors [3, 8, 12] who regard that strophanthidin is at the base of the jute glucosides (at least the principal ones).

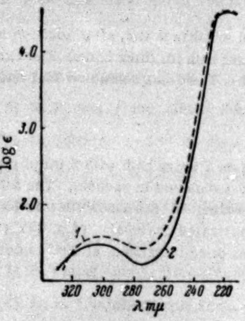

Fig. 1. Ultraviolet absorption spectra of olitoriside and its aglucone in alcohol.
1) Olitoriside; 2) olitoriside aglucone.

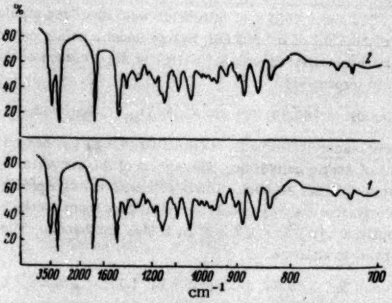

Fig. 2. Infrared absorption spectra of strophanthidin and olitoriside aglucone, taken in vaseline oil.
1) Strophanthidin; 2) olitoriside aglucone.

## EXPERIMENTAL

Isolation of olitoriside. Five kilograms of finely ground seeds of Corchorus olitorius L. was extracted with petroleum ether until completely defatted. The loss of weight in the extraction was 10%. The seeds, dried from the solvent residues, were subjected to a cold extraction with methyl alcohol (Legal's test was used for control). The methanolic extract was concentrated in vacuum at 45-50° to a volume of 1.5 liters and after the separation from a precipitate was reconcentrated to a volume of 700 ml. The sirupy mass was diluted with two volumes of acetone; precipitate "A" was formed thereby and this was separated and washed with ethanol. The methanol-acetone solution, combined with wash ethanol, was shaken with a suspension of 400 g of basic lead acetate in 500 ml of methanol. The resulting precipitate was separated and washed with methanol. The excess of lead ions was removed by addition to the filtrate of a saturated alcoholic solution of sodium chloride. The filtrate from lead chloride was evaporated in vacuum to a volume of 600 ml. The solution was shaken three times with an equal volume of ether, once with 200 ml of chloroform and was again concentrated to a volume of 300 ml. During a slow evaporation over several days (in a thermostat at 35-40°) of the thus-made extract, there began to precipitate from it some small joined crystals of olitoriside. The yield was 16 g.

The precipitate "A" (354 g) was triturated with 300 ml of ethanol; the mass crystallized on standing. After three recrystallizations from ethanol there was obtained a substance with m.p. 72°, which was identified as raffinose.

Olitoriside. The crude olitoriside (16 g) was dissolved in five parts of alcohol and the solution was passed through a column with aluminum oxide. The glucosides were eluted with ethanol. The eluate was concentrated in vacuum and the crystalline olitoriside was precipitated by addition of ether. The yield was 12 g. The recrystallization from a mixture of alcohol and ether was continued until the melting point and the specific rotation of the substance became constant after repeated recrystallizations.

The pure olitoriside has m.p. 204-206° (with decomposition), $[\alpha]^{22}D$ $-4.5° \pm 1°$ (c 4.8; methanol). Individual crystalline forms melted also at 222-224°.

Olitoriside is readily soluble in ethyl and methyl alcohols, difficultly soluble in chloroform and water, and insoluble in ethyl and petroleum ethers. Its color tests are: Lieberman – green color, Legal – orange-red color, Balier-Neuman – orange color, Raymond – blue color, Keller-Kiliani – dark green color, drop test on paper according to Frerejacque and Durgeat [13] with solution of vanillin and phosphoric acid in alcohol – a blue spot. The color reaction with 84% sulfuric acid with time: 0 min – dark green, 1 min – dark green, 2 min – brown-green, 5 min – brown, 30 min – brown, 1 hour – dirty brown.

The substance was dried in vacuum at 105° to constant weight prior to analysis.

Found %: C 60.45, 60.44; H 7.99, 7.82; $OCH_3$ 0.82, 0.81. $C_{35}H_{52}O_{14}$. Calculated %: C 60.33; H 7.52; $OCH_3$ 4.45.

0.3713 and 0.4667 g of olitoriside were dissolved separately in 30 ml of ethanol and, after addition to each sample of 39.4 ml of 0.1 N KOH, heated under a reflux condenser on a water bath for three hours. The excess alkali was back-titrated with 0.1 N HCl in the presence of phenolphthalein. There was consumed 34.1 and 32.8 ml of acid respectively.

Found: M 700.36, 707.12. $C_{35}H_{52}O_{14}$. Calculated: M 696.80.

Penta-acetylolitoriside. Olitoriside (0.5 g) was heated for two hours on a water bath with 5 ml of dry pyridine and 5 ml of acetic anhydride. The excess of the anhydride and pyridine was removed in vacuum. The solid residue was dissolved in hot alcohol. Small yellowish crystals precipitated after cooling of the alcoholic solution. The acetyl derivative was repeatedly recrystallized from alcohol (with use of activated charcoal). M.p. 229° (with decomposition), $[\alpha]^{22}D + 1.7 \pm 1°$ (c 1.344; methanol). The substance was dried in vacuum at 105° to constant weight prior to analysis.

Found %: C 59.44, 59.32; H 7.14, 7.17. $C_{45}H_{62}O_{19}$. Calculated %: C 59.59; H 6.89.

Hydrolysis of olitoriside. Strophanthidin. One g of olitoriside in 50 ml of methanol was heated under reflux after addition of 50 ml of 0.1 N sulfuric acid, on a boiling water bath for 25 minutes. Methanol was then removed in vacuum. Crystals precipitated on the following day from the remaining aqueous solution. The separated aglucone was recrystallized at first from aqueous alcohol, then from a mixture of alcohol and ether. It precipitated in this case in the form of rhombic prisms with m.p. 178° (with foaming); $[\alpha]^{25}D + 40.3 \pm 0.5°$ (c 2.603; methanol). Mixed melting point with an authentic sample of strophanthidin, obtained from cimarine, was 176-177°. The aglucone from olitoriside gave all the color tests which are characteristic of strophanthidin. All analyses were run with the hemihydrate form of the aglucone.

Found %: C 66.41; H 8.23; $H_2O$ 2.38. $C_{23}H_{32}O_6 \cdot \frac{1}{2} H_2O$. Calculated %: C 66.80; H 8.04; $\frac{1}{2} H_2O$ 2.18.

The equivalent weight was determined as indicated for olitoriside.

Found : M 419.14. $C_{23}H_{32}O_6 \cdot \frac{1}{2} H_2O$. Calculated: M 413.52.

Isostrophanthidin. The aglucone (0.5 g) from olitoriside was dissolved in 50 ml of 5% solution of potassium hydroxide in methanol. The solution was kept for three hours at room temperature after which it was diluted to twice the original volume with water, neutralized to weakly acidic reaction to Congo red with hydrochloric acid and heated for 5 minutes to 40-50°. After one day the solution precipitated thin plates which were difficultly soluble in alcohol. The crystals, recrystallized from alcohol, had m.p. 244-246°, $[\alpha]^{20}D + 23.3 \pm 2°$ (c 0.978; chloroform).

Acetylstrophanthidin. The aglucone (0.5 g) was heated for two hours on a boiling water bath with 5 ml of pyridine and 5 ml of acetic anhydride. The acetylation product, recrystallized from alcohol, had m.p. 241-242° and failed to give a depression in a mixed melting point with an authentic sample of acetylstrophanthidin. $[\alpha]^{20}D + 34.0 \pm 3°$ (c 0.696; methanol).

Found %: C 67.05, 67.30; H 7.66, 7.56. $C_{25}H_{34}O_7$. Calculated %: C 67.24; H 7.67.

Strophanthidin phenylhydrazone. The aglucone (0.5 g) in 10 ml of alcohol was mixed with the solution of 1.0 g of phenylhydrazine hydrochloride and 1.5 g of sodium acetate in 10 ml of water. The mixture was heated on a water bath for 30 minutes. Crystals appeared on cooling. The phenylhydrazone, recrystallized from 80% alcohol, precipitated in the form of colorless prisms, which after drying over phosphoric anhydride, had m.p. 241-243° (with decomposition).

Found %: N 5.07, 5.04. $C_{29}H_{38}O_5N_2$. Calculated %: N 5.66.

## SUMMARY

1. A new steroidal glucoside – olitoriside, $C_{35}H_{52}O_{14}$ – was isolated from seeds of Corchorus olitorius L. (fam. Tiliaceae) and was characterized.

2. Olitoriside is a biocide and under the influence of acids hydrolyzes to a sugar residue and strophanthidin.

3. New data are supplied which confirm the identity of corchorine and strophanthidin.

## LITERATURE CITED

[1] Tsuno, Monatsh. Tierheilk., 6, 455 (1896).

[2] N. K. Sen, J. Ind. Chem. Soc., 7, 83, 905 (1930); 8, 651 (1931).

[3] G. Soliman and W. Saleh, J. Chem. Soc., 1950, 2198.

[4] A. Alam, A. Khalique and M. Ahmed, Cur. Sci., 23, 332 (1954).

[5] M. Moslemuddin and M. Ahmed. J. Ind. Chem. Soc., 32, 577 (1955).

[6] N. Saha and K. N. Choudhury, J. Chem. Soc. 121, 1044 (1922).

[7] P. Karrer and P. Banerjea, Helv. Chim. Acta, 32, 2385 (1949).

[8] D. H. Chaudbury and P. C. Dutta, J. Ind. Chem. Soc., 28, 167 (1951).

[9] M. A. Khalique and M. Ahmed, Nature, 170, 1019 (1952); J. Org. Ch., 19, 1523 (1954).

[10] N. K. Sen and J. K. Chakravarti, Sci. and Cult., 19, 102 (1953); J. Am. Chem. Soc., 76, 2390 (1954).

[11] G. V. Lazur'evskii and V. K. Orlov. Sci. Notes of Kishinev State Univ., 14, 57 (1954).

[12] M. Frerejacque and M. Durgeat, C. r., 238, 507 (1954).

[13] M. Frerejacque and M. Durgeat, C. r., 236, 410 (1953).

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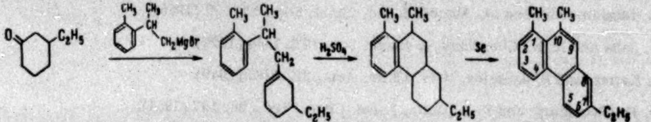
# A STUDY OF ACONITE ALKALOIDS

## XII. STRUCTURE OF THE HYDROCARBON $C_{18}H_{18}$ AND THE POSSIBLE FORMULA OF SONGORINE

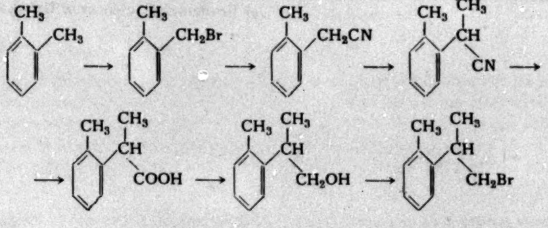
A. D. Kuzovkov

Earlier [1] we prepared a hydrocarbon $C_{18}H_{18}$ in dehydrogenation of songorine with selenium. We accomplished the synthesis of this substance according to the following scheme:

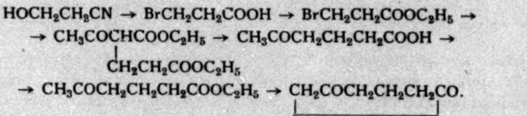


A mixture of isomers, differing in the position of the double bond, may be formed in the dehydration of the tertiary alcohol formed in the Grignard reaction. In this case, after cyclization and the subsequent dehydrogenation, there may form not only the expected 1,10-dimethyl-7-ethylphenanthrene, as indicated on the above scheme, but also 1,10-dimethyl-5-ethylphenanthrene. The substance isolated by us after the dehydrogenation was identical with the hydrocarbon $C_{18}H_{18}$ formed in dehydrogenation of songorine. The position of the ethyl group in this substance at the $C_7$ location in the phenanthrene nucleus was established by the previously run [2] oxidation of the hydrocarbon $C_{18}H_{18}$ to biphenyl-2,3,2',4'-tetracarboxylic acid.

1-Bromo-2-o-tolylpropane was prepared starting with o-xylene:



For the synthesis of 1-ethyl-3-cyclohexanone we used 1,3-cyclohexanedione as the starting material, this being prepared as the result of the following reactions which are described in the literature [3]:

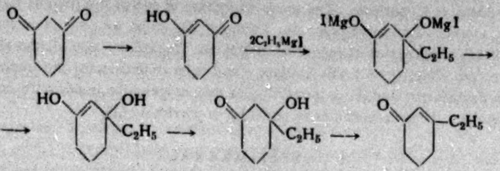


$$\mathrm{HOCH_2CH_2CN \rightarrow BrCH_2CH_2COOH \rightarrow BrCH_2CH_2COOC_2H_5 \rightarrow}$$

$$\mathrm{\rightarrow \underset{\displaystyle \overset{|}{CH_2CH_2COOC_2H_5}}{CH_3COCHCOOC_2H_5} \rightarrow CH_3COCH_2CH_2CH_2COOH \rightarrow}$$

$$\mathrm{\rightarrow CH_3COCH_2CH_2CH_2COOC_2H_5 \rightarrow \underbrace{CH_2COCH_2CH_2CH_2CO}.}$$

It is known [4] that 1,2-cyclohexanedione undergoes the Grignard reaction in the enolic form. This reaction proceeds analogously if one takes 1,3-cyclohexanedione:



1-Ethyl-3-cyclohexanone was prepared by hydrogenation of ethylcyclohexenone over Raney nickel catalyst and the product was characterized in the form of its semicarbazone.

The clarification of the structure of hydrocarbon $C_{18}H_{18}$ permitted us to generalize the known properties of songorine and to make some suppositions about the structure of this alkaloid.

The results of analysis of songorine (m.p. 201-203°) correspond to the formula $C_{21}H_{29}O_3N$ as well as to the formula $C_{22}H_{31}O_3N$. Formaldehyde is cleaved in ozonolysis of songorine, this fact indicating the presence of a terminal methylene group. In reduction of songorine by sodium borohydride there was obtained a dihydro derivative with m.p. 163-165° (picrate, m.p. 232°) in which the oxo group is reduced to the hydroxyl. In the catalytic hydrogenation of songorine there is formed, besides dihydrosongorine with m.p. 205-207° [5], a substance which is isomeric with songorine – isosongorine (m.p. 193-195°).

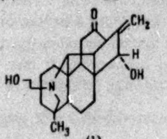
A band of the isolated oxo group present in a six-membered ring (1708 $cm^{-1}$) is found in the infrared spectrum of songorine. The spectrum of isosongorine indicates the presence of two oxo groups (1708 and 1740 $cm^{-1}$); one of these is located in a six-membered, the other in a five-membered ring. The appearance of a new oxo group in isosongorine is explained [6] by the transformation of $-CH(OH)-\underset{|}{C}=CH_2$ group into $-CO-\underset{|}{CH}-CH_3$ group.

In the ultraviolet spectrum of songorine there is observed absorption in the region of 290 mμ ($\lambda_{max}$ 290 mμ, log ε 2.6) which is more intense than would be expected in the presence of but a single isolated oxo group. Reduction of a double bond or an oxo group leads to a weakening of absorption: absorption of dihydrosongorine in this region ($\lambda_{max}$ 285 mμ, log ε 1.6) corresponds to that of ordinary ketones; the dihydro derivative with m.p. 163-165° does not have absorption maxima in this region. One may suppose the presence of the grouping of β,γ-unsatured ketone in songorine [7].

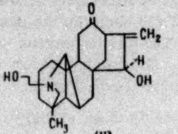
The recently published paper [8] about the separation of the alkaloid napelline into two new alkaloids – napelline and napellonine – may be considered. The properties of the latter substance are quite close to the properties of songorine which gives us the opportunity to make a supposition about the identity of these alkaloids.

In the infrared spectrum of napellonine, $C_{22}H_{31}O_3N$ (m.p. 212°) there is a band of the oxo group in a six-membered ring (1708 $cm^{-1}$); in the ultraviolet spectrum there is observed an abnormally high (for an isolated oxo group) absorption with $\lambda_{max}$ 290 mμ (log ε 2.6). By reduction of napellonine with lithium aluminum hydride there was obtained napelline $C_{22}H_{33}O_3N$ with m.p. 166° (picrate, m.p. 238°) On hydrogenation of napellonine there is observed its conversion into a diketone $C_{22}H_{31}O_3N$ with m.p. 203°, containing oxo groups in the six-membered (1707 $cm^{-1}$) and the five-membered rings (1733 $cm^{-1}$). Hydrocarbon $C_{18}H_{18}$ forms in dehydrogenation of napelline [9] and we have already indicated [1] the similarity of this hydrocarbon with the hydrocarbon formed in dehydrogenation of songorine.

The hypothetical formula (I) has been suggested [8] for napellonine:



(I)



(II)

The identity of napellonine and songorine permits us to consider formula (I) from the viewpoint of the results of study of songorine structure. The formation of 1,10-dimethyl-7-ethylphenanthrene in the dehydrogenation of songorine confirms the presence of substituents at the $C_1$ position of perhydrophenanthrene nucleus and the joining of the five-membered ring at $C_7$ position. The proposed joining of one of the rings at $C_8$ is improbable; the joining of this ring at $C_{10}$ appears to be more probable. Formula (II), which we propose as one of the possibilities, explains the results of dehydrogenation of songorine best of all. It explains also all the above-listed properties of songorine and napellonine. Starting with this formula, one begins to understand the impossibility of the second stage of the Hofmann degradation and the impossibility of dehydrogenation under mild conditions without a cleavage of the carbon skeleton; these facts had been noted by us previously [1].

## EXPERIMENTAL

α-o-Tolylpropionic acid. To a suspension of 34 g of sodium in 1000 ml of dry ether there was added gradually 134 g of o-tolylacetonitrile. After termination of the violet reaction, the mixture was refluxed for 30 minutes, after which there was added to it 150 g of methyl iodide with ice cooling. After refluxing for 30 minutes, the sodium residues were destroyed by addition of alcohol and the mixture was poured on ice; the reaction product was extracted with ether. The extract was washed with water, dried with sodium sulfate and evaporated. There was obtained 56 g of the nitrile with b.p. 150-160° (40 mm). The 56 g of the nitrile was added to a solution of 104 ml of concentrated sulfuric acid in 70 ml of water. The mixture was heated carefully. At the start of a violent reaction, the reaction flask was cooled for a while, after which the mixture was heated at reflux for 30 minutes. The reaction product was extracted with ether. The extract was washed with water, dried with sodium sulfate and evaporated. After crystallization from heptane there was obtained 26 g of the acid with m.p. 92-94°.

Found %: C 72.76, 72.84; H 7.46, 7.41. $C_{10}H_{12}O_2$. Calculated %: C 73.14; H 7.37.

Methyl-o-tolylcarbinol. The solution of 26 g of α-o-tolylpropionic acid in 0.75 liter of dry ether was gradually added to a solution of 4.6 g of lithium aluminum hydride in 0.75 liter of dry ether. The mixture was refluxed for two hours. There was obtained 19 g of methyl-o-tolylcarbinol with b.p. 135-136° (24 mm).

Found %: C 79.80; H 9.41. $C_{10}H_{14}O$. Calculated %: C 79.96; H 9.39.

1-Bromo-2-o-tolylpropane. To 19 g of methyl-o-tolylcarbinol there was added, with cooling, 19 g of phosphorus tribromide. After heating for 30 minutes at 100°, the mixture was poured on ice and the reaction product was extracted with ether. There was obtained 20 g of the bromide with b.p. 100-101° (5 mm).

Found %: Br 37.41, 37.55. $C_{10}H_{13}Br$. Calculated %: Br 37.50.

1-Ethyl-3-cyclohexanone. A suspension of 32 g of 1,3-cyclohexanedione with m.p. 101-103° (from ethyl acetate) was added with cooling to the solution of ethylmagnesium iodide (from 16.3 g of magnesium and 108 g of ethyl iodide) in 500 ml of ether. The mixture was refluxed for two hours, after which it was poured on ice, the mixture was acidified with concentrated hydrochloric acid and the reaction product extracted with ether. There was obtained 16 g of ethylcyclohexenone with b.p. 135-140° (50 mm). The latter was dissolved in 16 ml of methanol and was hydrogenated with Raney nickel catalyst under a slight pressure of hydrogen. The reaction product was distilled in vacuum; yield — 9.5 g; b.p. 195-205° (15 mm).

Found %: C 75.58; H 11.64. $C_8H_{14}O$. Calculated %: C 76.13; H 11.18.

The semicarbazone of 1-ethyl-3-cyclohexanone was prepared by the usual method; m.p. 169-171° without recrystallization.

1,10-Dimethyl-7-ethylphenanthrene. To 50 ml of ethereal solution of $o\text{-}CH_3C_6H_4CH(CH_3)CH_2MgBr$ (from 16.6 g of 1-bromo-2-o-tolylpropane and 1.9 g of magnesium) there was added with cooling an ethereal solution of 1-ethyl-3-cyclohexanone. The reaction mixture was refluxed for two hours, after which it was poured on ice. The reaction product was extracted with ether and distilled in vacuum. There was obtained 5.2 g of the condensation product with b.p. 195-205° (15 mm). To this there was added a cooled mixture of 11 g of concentrated sulfuric acid and 2 ml of water. The reaction mixture was shaken periodically, left for one hour at room temperature and finally poured on ice. The reaction product was extracted with ether and distilled in vacuum. There was obtained 3.9 g of dimethyloctahydrophenanthrene with b.p. 195-205° (15 mm).

Dimethylethyloctahydrophenanthrene (3.9 g) was heated with 3 g of selenium at 340° (bath temperature) for four hours. The reaction product was dissolved in hexane and chromatographed on aluminum oxide. From the zone which fluoresced strongly in ultraviolet light there was eluted with ether 0.5 g of a substance whose picrate melted at 124-125° after several recrystallizations from alcohol. The solution of the picrate in ether was passed through aluminum oxide. After evaporation of the eluate, the residue crystallized. As the result of recrystallization from methanol, alcohol and again, methanol, there was obtained a colorless substance with m.p. 78-79°; no depression was observed in the mixed melting point with the hydrocarbon $C_{18}H_{18}$ obtained from songorine. The hydrocarbon yielded a picrate with m.p. 131-132°; its mixture with the picrate of the hydrocarbon from songorine melted at the same temperature. Infrared absorption spectra of these two picrates were completely coincident.

Ozonolysis of songorine. A stream of ozonized oxygen was passed for nine minutes through a solution of 1 g of songorine in 28.8 ml of 0.1 N hydrochloric acid at 0°; during this period about 0.03 millimoles of ozone was absorbed. The solution was evaporated in vacuum at a temperature below 30°. Formaldehyde derivative of dimethylcyclohexanedione was obtained from the distillate; this melted at 183-184°; a mixed melting point with an authentic specimen of the formaldehyde derivative showed no depression. In a parallel experiment on ozonization of dihydrosongorine no formaldehyde was formed. From the residue after evaporation in vacuum of the solution after ozonization of songorine there were isolated an uncrystallizable substance (0.5 g) and an uncrystallizable amino acid (0.5 g). From the latter there was obtained an uncrystallizable ethyl ester, after esterification by the Fischer method.

Catalytic hydrogenation of songorine. Five g of songorine in a mixture of 10 ml of alcohol and 30 ml of 5% hydrochloric acid was hydrogenated with platinum catalyst prepared from 0.5 g of platinum oxide. After evaporation of alcohol, making the solution basic with ammonia and extraction with ether, there was extracted a base with m.p. 163-176°. This substance was treated with 25 ml of boiling benzene. From the insoluble residue, after recrystallization from alcohol, there was obtained 1.5 g of dihydrosongorine. From the benzene solution there was isolated a base which, after numerous recrystallizations from methanol, yielded isosongorine with m.p. 193-195°. Its mixture with dihydrosongorine melted at 170-178°.

Found %: C 73.93; H 8.62; N 3.95; OH 6.0. $C_{22}H_{31}O_3N$. Calculated %: C 73.93; H 8.74; N 3.92; OH 4.79.

Reduction of songorine with sodium borohydride. To a solution of 0.8 g of songorine in methanol there was added 0.8 g of sodium borohydride with ice cooling. The mixture was refluxed for two hours, then evaporated in vacuum. To the residue there was added some water and an excess of ammonia, after which the reaction product was extracted with ether. There was obtained a base which crystallized after prolonged standing. M.p. 163-165° (from acetone); hydrobromide, m.p. 216-216.5°; picrate, m.p. 332°

## SUMMARY

1. 1,10-Dimethyl-7-ethylphenanthrene was synthesized and the identity of this hydrocarbon with hydrocarbon $C_{18}H_{18}$ obtained from dehydrogenation of songorine was established.

2. A hypothetical formula of the structure of songorine was suggested.

## LITERATURE CITED

[1] A. D. Kuzovkov, J. Gen. Chem. 25, 2006 (1955).*

[2] A. D. Kuzovkov, J. Gen. Chem. 28, 558 (1958).*

[3] Syntheses of Organic Preparations. Vol. 1, pp. 133, 543; vol. 2, p. 580 (1949);** W. H. Bentley and W. H. Perkin, J. Chem. Soc. 69, 1510 (1896); D. Vorländer. Lieb. Ann. 294, 253 (1896).

[4] L. W. Butz and co-workers, J. Org. Ch. 12, 122 (1947).

[5] S. Iu. Iunusov, J. Gen. Chem. 18, 515 (1948).

[6] T. Sugasawa, Pharm. Bull. 4, 6 (1956)

[7] R. C. Cookson and N. S. Wariyar, J. Chem. Soc. 1956, 2302.

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*Original Russian pagination. See C.B. translation.

**In Russian.

[8] K. Wiesner, Z. Valenta, J. F. King, R. B. Maudgal, L. G. Humber and Ito Sho, Chem. and Ind., 1956, No. 6, 173.

[9] W. A. Jacobs, and L. C. Craig, J. Biol. Ch. 1943, 611 (1942).

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# SYNTHESES OF VINYL MONOMERS

## IV. FLUORINE-SUBSTITUTED ACRYLATES

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The number of known fluoro-substituted acrylates is small [1]. Among alkyl methacrylates containing fluorine atoms in the alkyl group, there has been described only β,β,β-trifluoroethyl methacrylate [2]. Among the compounds substituted with fluorine in the acid portion of the molecule there have been prepared: α-trifluoromethylacrylates [3], α-fluoro-, β,β-difluoro- and trifluoroacrylic acids [4]. We synthesized an entire series of fluorinated acrylates whose description is given below. Starting with β-fluoroethyl and β,β,β-trifluoroisopropyl alcohols and the chloride of methacrylic acid, we prepared by conventional method: trifluoroisopropyl and β-fluoroethyl methacrylates. The last compound, as indicated above, had been previously mentioned only in a patent and for this reason its more detailed description is given by us in the experimental section.

Attempts to prepare fluoromethyl methacrylate from chloro- and bromo-methyl methacrylates by exchange of the indicated atoms of halogens for fluorine with the aid of potassium fluoride or mercury fluoride failed to give positive results. We failed to isolate any fluoromethyl acrylate from the reaction products. We also failed to obtain this substance by the way of condensation of the fluoride of methacrylic acid with formaldehyde, a reaction analogous to that realized in the syntheses of chloro- and bromomethyl methacrylates described by us [5]. From acrylates containing fluorine in the acid portion of the molecule we did synthesize methyl α-fluoromethyl- and α-difluoromethylacrylates and some of their derivatives. The synthesis of these compounds was realized through the scheme below:

$$CH_3COCHX_2 \xrightarrow{HCN} CH_3COH(CN)CHX_2 \xrightarrow{H_2O} CH_3COH(COOH)CHX_2 \xrightarrow[CH_3OH]{}$$

$$\longrightarrow CH_3COH(COOCH_3)CHX_2 \xrightarrow{(CH_3CO)_2O} CH_3C(OCOCH_3)(COOCH_3)CHX_2 \longrightarrow$$

$$\xrightarrow[-CH_3COOH]{500^\circ} CH_2{=}C(CHX_2)COOCH_3,$$

where X = F or H.

All the intermediate products in these syntheses (cyanohydrins, α-hydroxypropionic acid and their esters and acetates), containing fluoro- and difluoromethyl groups, were isolated and characterized.

The initial fluoro- and difluoroacetones were prepared, in contrast to the previously described more complex methods of synthesis, by the exchange reaction of chloro- and dichloroacetones with potassium fluoride in a solution of diethylene glycol; the properties of the acetone fluorides synthesized in this manner did not differ from the previously described properties of fluoro- and difluoroacetones.

## EXPERIMENTAL

I. β-Fluoroethyl methacrylate. A mixture of 49.9 g of the chloride of methacrylic acid, 30.5 g of ethylene fluorohydrin and 0.06 g of hydroquinone was heated for three hours at 90°. The product was distilled in vacuum, whereby there was collected 44 g of a fraction boiling within the limits of 40-53° at 63 mm. After a second distillation of this fraction there was isolated 27.3 g of β-fluoroethyl methacrylate with b.p. 48-49° at 15 mm.

$d^{20}_4$ 1.0904, $n^{20}D$ 1.4200.

Found %: C 54.27; H 6.82; F 13.28, M 132.1. $C_6H_9O_2F$. Calculated %: C 54.5; F 14.3; M 132.

II. Trifluoroisopropyl methacrylate. To 14.4 g of β,β,β-trifluoroisopropyl alcohol there was added dropwise 12 g of the chloride of methacrylic acid at 50-60°. After completion of the addition, the reaction mixture was heated for 1.5-2 hours longer at the indicated temperature. Then the mixture was washed three times with water, dried with calcium chloride and distilled. There was obtained 7.5 g (36.5%) of trifluoroisopropyl methacrylate with b.p. 114°.

$d^{20}_4$ 1.1308, $n^{20}D$ 1.3677, $MR_D$ 35.47; calculated 36.17.

Found %: C 45.68; H 5.29; F 31.75. $C_7H_9O_2F_3$. Calculated %: C 46.2; H 4.43; F 31.18.

III. Methyl α-fluoromethylacrylate. a) Fluoroacetone. A mixture of 93.5 g of calcined powdered potassium fluoride and 265 g of diethylene glycol was heated in an oil bath with stirring to 170°, after which 150 g of chloroacetone was added to it dropwise. The resulting fluoroacetone was distilled and collected in a receiver in the amount of 40-44 g. The collected liquid was dried with sodium sulfate and distilled. There was isolated 26 g of fluoroacetone with b.p. 73.5-74.5°, $d^{20}_4$ 1.065, $n^{20}D$ 1.3702.

b) Fluoroacetone cyanohydrin. A solution of 41 g of potassium cyanide in 160 ml of water was cooled to 0°. With stirring, 42 g of fluoroacetone was introduced dropwise, after which 240 ml of 25% sulfuric acid was added slowly with cooling to 0°. The temperature of the reaction mixture was maintained within the limits of 0-10°. After completion of addition of sulfuric acid, the reaction mixture was stirred for 30 minutes longer and was allowed to stand overnight, after which it was extracted 5-6 times with 125 ml portions of ether. The ethereal extracts were combined, dried with sodium sulfate, the ether was distilled from them on a water bath and the residue was distilled in vacuum. There was obtained 40.8 g (72%) of fluoroacetone cyanohydrin with b.p. 73.5-74 at 3 mm.

$d^{20}_4$ 1.1169, $n^{20}D$ 1.3995.

Found %: C 47.85; H 6.42; N 14.48; F 18.19. $C_4H_6ONF$. Calculated %: C 46.8; H 5.82; N 13.6; F 18.45.

c) α-Fluoromethyl-α-hydroxypropionic acid. Into 33.5 g of concentrated sulfuric acid there was added dropwise with stirring 40.8 g of fluoroacetone cyanohydrin. The temperature, which rises during this operation, reaching 70-80°, was regulated by the rate of addition of the fluoroacetone cyanohydrin. To the cooled mixture there was gradually added 390 ml of water and the mixture was heated on a boiling water bath for six hours, after which the mixture was evaporated in a porcelain dish until it began to crystallize. After cooling, the resulting crystals of the acid were filtered off, dried (43-45 g) and recrystallized from benzene. There was obtained 20 g of pure α-fluoromethyl-α-hydroxypropionic acid in the form of readily water soluble colorless crystals with m.p. 94.5-95.5°.

Found %: C 39.83; H 7.37; F 17.36. $C_4H_7O_3F$. Calculated %: C 39.3; H 5.75; F 15.6.

d) Methyl α-fluoromethyl-α-hydroxypropionate. A mixture of 108 g of α-fluoromethyl-α-hydroxypropionic acid, 75.5 g of anhydrous methyl alcohol and 3 ml of concentrated sulfuric acid was refluxed on a water bath for 16-17 hours. The excess methanol was distilled and the residue was distilled in vacuum whereby there was obtained 86.4 g (72.3%) of methyl α-fluoromethyl-α-hydroxypropionate in the form of colorless liquid with a pleasant odor with b.p. 53-54° at 7 mm, the product being readily soluble in water.

$d^{20}_{20}$ 1.1791, $n^{20}D$ 1.4065.

Found %: C 45.05; H 4.15; F 13.8. $C_5H_9O_3F$. Calculated %: C 44.3; H 6.6; F 13.98.

e) Methyl α-fluoromethyl-α-acetoxypropionate. A mixture of 86.4 g of methyl α-fluoromethyl-α-hydroxypropionate, 110 g (70% excess) of acetic anhydride and 8.5 g of fused sodium acetate was heated on a boiling water bath for 5-6 hours. After cooling, the reaction mixture was poured into 125 ml of ice water, separated, dried with magnesium sulfate and distilled in vacuum. There was obtained 85.7 g (76.5%) of methyl α-fluoromethyl-α-acetoxypropionate in the form of water insoluble colorless liquid with b.p. 65-66.5° at 5 mm.

$d^{20}_{20}$ 1.1757, $n^{20}D$ 1.4076.

Found %: C 45.63; H 7.02; F 9.93. $C_7H_{11}O_4F$. Calculated %: C 44.7; H 6.35; F 10.7.

f) Methyl α-fluoromethylacrylate. Seventy g of methyl α-fluoromethyl-α-acetoxypropionate was passed through a quartz tube (450 mm long and 25 mm in diameter; heated zone – 400 mm) packed with pieces of hard glass tubing and preliminarily flushed with dry nitrogen; the tube was heated to 500° while the ester was added at the rate of 1 g per minute.

The pyrolysis products were collected in a receiver cooled by a mixture of ice and salt. There was obtained 66 g of pyrolyzate which was washed four times with a mixture of 10% solution of sodium bicarbonate and saturated sodium chloride solution, dried with anhydrous calcium chloride and distilled with addition of 0.1% of hydroquinone. There was obtained 18.5 g (40%) of methyl α-fluoromethylacrylate in the form of a transparent colorless liquid with a sharp, irritating odor; insoluble in water; b.p. 123-125°.

$d^{20}_{20}$ 1.1084, $n^{20}$D 1.4092.

Found %: C 51.02; H 6.29; F 17.35. $C_5H_7O_2F$. Calculated %: C 50.8; H 5.9; F 16.05.

IV. Methyl α-difluoromethylacrylate. a) Difluoroacetone. A mixture of 85 g of calcined powdered potassium fluoride and 395 g of diethylene glycol was stirred for ten minutes in a three-necked flask, after which there was added 80 g of dichloroacetone and the mixture was heated in an oil bath to 185-195°. The resulting difluoroacetone distilled at 50-60° (in the vapor) and was collected in the receiver in the volume of 5-8 g. By distillation there was isolated unsym-difluoroacetone with b.p. 42.5-43°, $n^{20}$D 1.3570, $d^{20}_{20}$ 1.238.

b) Difluoroacetone cyanohydrin. From 20 g of difluoroacetone, after treatment with sodium cyanide as in experiment IIIb, there was obtained 14.4 g (57%) of difluoroacetone cyanohydrin with b.p. 70.5-71° at 9 mm.

$n^{20}$D 1.3750, $d^{20}_{20}$ 1.2358.

Found %: C 41.3; H 5.78; N 11.56; F 34.2. $C_4H_5ONF_2$. Calculated %: C 39.7; H 4.15; N 11.65; F 31.3.

c) α-Difluoromethyl-α-hydroxypropionic acid. Difluoroacetone cyanohydrin (12.9 g) was hydrolyzed as in experiment IIIc. The resulting aqueous solution of the acid was extracted several times with ether, the extract was dried with sodium sulfate, the ether was distilled and there was obtained 11.7 g of crude α-difluoromethyl-α-hydroxypropionic acid. By recrystallization from benzene there was obtained 11.6 g of the pure product with m.p. 87.5-88.5°.

Found %: C 35.01; H 4.78; F 25.93. $C_4H_6O_3F_2$. Calculated %: C 34.3; H 4.3; F 27.2.

d) Methyl α-difluoromethyl-α-hydroxypropionate. Nine g of α-difluoromethyl-α-hydroxypropionic acid was methylated as described in experiment IIId, whereby there was obtained 5.7 g (60%) of methyl-α-difluoromethylpropionate (should be -α-hydroxypropionate) in the form of a colorless, transparent, water-soluble liquid with b.p. 42-43.5° at 3 mm.

$d^{20}_{20}$ 1.2801, $n^{20}$D 1.3896.

Found %: C 40.56; H 6.01; F 24.45. $C_5H_8O_3F_2$. Calculated %: C 39.0; H 5.9; F 24.7.

e) Methyl α-difluoromethyl-α-acetoxypropionate. Five g of methyl α-difluoromethyl-α-hydroxypropionate was acetylated with acetic anhydride, as in experiment IIIe. There was obtained 3.7 g (58.5%) of methyl α-difluoromethyl-α-acetoxypropionate with b.p. 54.5-56° at 5 mm.

$d^{20}_{20}$ 1.2445, $n^{20}$D 1.3922.

Found %: C 43.56; H 5.43; F 18.22. $C_7H_{10}O_4F_2$. Calculated %: C 42.8; H 5.1; F 19.4.

f) Methyl α-difluoromethylacrylate. Twenty g of methyl α-difluoromethyl-α-acetoxypropionate was pyrolyzed and treated as in experiment IIIf. There was obtained 2.8 g (20%) of methyl α-difluoromethylacrylate in the form of a colorless, transparent liquid with a sharp irritating odor, with b.p. 46.5-47° at 40 mm.

$d^{20}_{20}$ 1.1830, $n^{20}$D 1.3900.

Found %: C 45.57; H 5.5; F 26.8. $C_5H_6O_2F_2$. Calculated %: C 44.25; H 4.4; F 27.9.

## SUMMARY

There was described the preparation and the properties of methyl α-fluoromethyl- and methyl α-difluoromethylacrylates, prepared from fluoro- and difluoroacetone, respectively, through the nitriles and other derivatives of α-fluoromethyl- and α-difluoromethyl-α-hydroxypropionic acids.

## LITERATURE CITED

[1] D. Codding, F. Reid, A. Ahlbrecht and G. Smith, J. Polym. Science, 15, 515 (1955); U.S. Patent 2628958 (1953); Chem. Abstr. 47, 5728 (1953).

[2] Brit. Patent 580665 (1946); Chem. Abstr. 42, 2071 (1947); U.S. Patent 2628958 (1953); Chem. Abstr. 47, 5728 (1953).

[3] H. Buxton, M. Stacly and G. Tatlow, J. Chem. Soc., 1954, 366.

[4] A. Henne, Ch. Fox, J. Am. Chem. Soc., 76, 479 (1954); U. S. Patent 2454663 (1948); Chem. Abstr. 43, 2223 (1949).

[5] A. Iakubovich, V. Razumovskii, S. Rozenshtein and Z. Vostrukhina, J. Gen. Chem., 28, 1930 (1958).*

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# SYNTHESES OF VINYL MONOMERS

## V. SYNTHESES OF CYANO-SUBSTITUTED ACRYLATES

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Among the considerable number of esters of acrylic and methacrylic acid described in the literature the esters of cyano-substituted alcohols still remained among the poorly studied ones. By the reaction of an aqueous solution of formaldehyde, sodium cyanide and the chloride of the acid, there were prepared the cyanomethyl esters of acrylic and methacrylic acids [1]. Also were described the α-cyanoethyl and α-cyanoisopropyl esters of acrylic acid [2].

The use of cyanomethyl, β-cyanoethyl and α-cyanoisopropyl esters of methacrylic acid was recommended in the patent literature [3] for the preparation of their polymers and copolymers. However the preparation of the monomeric esters and their properties were described far from adequately. We studied these esters in detail and also prepared the previously undescribed α-cyanoethyl, α-cyanobenzyl and p-cyanophenyl esters of methacrylic acid. We used the known methods ([1] and others) for the synthesis of cyanoalkyl methacrylates.

p-Cyanophenyl methacrylate was prepared by the reaction of methacrylyl chloride with p-cyanophenol analogously to other similar syntheses of aryl methacrylates [4].

Along with the indicated cyano-substituted esters, we synthesized the previously undescribed cyano-substituted methylamide of methacrylic acid $CH_2=C(CH_3)CONHCH_2CN$, by the reaction of methacrylyl chloride with free aminoacetonitrile in acetone, as well as derivatives of α-cyanoacrylic acid, specifically its nitrile – vinylidene-cyanide – and the methyl ester.

Vinylidene cyanide was prepared by us by the method described in the literature [5], with the initial 1,1,3,3-tetracyanopropane being prepared according to [6]. However we met with considerable difficulties in the course of realization of these syntheses.

In connection with this, we altered somewhat the procedures which were recommended in the literature.

The literature data on the esters of α-cyanoacrylic acid are quite limited. The preparation and the properties of methyl and other esters of α-cyanoacrylic acid are described only briefly in patents [7].

We prepared methyl α-cyanoacrylate by means of both methods indicated in the patents, starting in one case with methyl cyanoacetate and chloromethyl acetate, in the other with methyl cyanoacetate and formaldehyde.

$$NaCH(CN)COOR \xrightarrow[-NaCl]{+CH_3COOCH_2Cl} CH_3COOCH_2CH(CN)COOR \xrightarrow{-CH_3COOH}$$

$$\longrightarrow CH_2{=}C(CN)COOR,$$

$$CH_2(CN)COOR \xrightarrow[\text{piperidine}]{CH_2O} CH_2{=}C(CN)COOR + H_2O$$

In working by both methods we obtained, despite the indications of the first patent, not the monomeric methyl α-cyanoacrylate but a semisolid partly polymerized product. For preparation of the monomeric ester we subjected this to depolymerization by heating in the presence of phosphorus pentoxide. The second method was more simple and conveneint, yielding also the better yields of methyl α-cyanoacrylate.

## EXPERIMENTAL

1. α-Cyanoethyl methacrylate. a) To a solution of 35 g of sodium cyanide (90%) in 70 ml of water there was added at 6-15° with stirring 30 g of acetaldehyde followed by 90 g of methacrylyl chloride. After this the mixture was stirred for one hour longer without cooling. The oily layer was extracted with ether, the extract washed with a solution of sodium carbonate, 3% solution of hydrochloric acid and 3% solution of sodium bicarbonate, after which it was dried over calcium chloride. After distillation of ether, the product, inhibited with phenyl-β-naphthylamine, was distilled in vacuum. There was obtained 63 g (66% on acetaldehyde) of α-cyanoethyl methacrylate.

B.p. 78-80° at 12 mm, $d^{20}_4$ 1.0064, $n^{20}D$ 1.4329. $MR_D$ 35.88; calc. 35.48.

Found %: C 59.24, 58.95; H 6.93, 6.96; N 10.05, 9.85. $C_7H_9O_2N$. Calculated %: C 60.4; H 6.47; N 10.0.

b) A mixture of 24 g of acetaldehyde cyanohydrin [8], 40 g of methacrylyl chloride and 0.1 g of hydroquinone was kept at gentle reflux for one hour and after cooling to room temperature during 1.5 hours, was distilled in vacuum. The fraction with b.p. 60-100° at 10 mm was washed with a saturated solution of sodium chloride, dissolved in ether and the solution was dried over calcium chloride. After distillation there was obtained 16.4 g of α-cyanoethyl methacrylate with b.p. 63-64° at 8 mm; $d^{20}_4$ 1.0065; $n^{20}D$ 1.4327. The yield was 35% calculated on acetaldehyde cyanohydrin.

2. α-Cyanobenzyl methacrylate. The synthesis was run by the method described in 1 a. From the solution of 31.7 g of sodium cyanide (100%) in 70 ml of water, 70 g of benzaldehyde and 86 g of freshly distilled methacrylyl chloride there was obtained 69.4 g (52% on benzaldehyde) of α-cyanobenzyl methacrylate.

b.p. 123-125° at 1 mm, $d^{20}_4$ 1.1057, $n^{20}D$ 1.5170. $MR_D$ 54.99; calc. 54.97.

Found %: C 71.70, 71.57; H 5.22, 5.28; N 7.75, 7.50. $C_{12}H_{11}O_2N$. Calculated %: C 71.64; H 5.47; N 6.96.

3. α-Cyanoisopropyl methacrylate. A mixture of 35 g of acetone cyanohydrin, 50 g of methacrylyl chloride and 0.3 g of hydroquinone was kept at gentle reflux for one hour and then worked up as in experiment 1b.

There was obtained 29.6 g of α-cyanoisopropyl methacrylate (58% on acetone cyanohydrin).

B.p. 85-86° at 9 mm, $d^{20}_4$ 0.9904, $n^{20}D$ 1.4330. $MR_D$ 40.15; calc. 40.10.

According to data [3]: b.p. 72-73° at 4 mm, $n^{25}D$ 1.4305.

4. β-Cyanoethyl methacrylate. A mixture of 36 g of ethylene cyanohydrin, 60 g of methacrylyl chloride and 0.1 g of hydroquinone was heated at 90° for 30 minutes after which it was subjected to vacuum distillation. There were collected two fractions: 1st up to 95° at 3 mm, 9.6 g, and 2nd b.p. 96-105° at 3 mm, 47 g. After the second distillation of the second fraction there was obtained 41.3 g (58% on ethylene cyanohydrin) of β-cyanoethyl methacrylate.

B. p. 95-97° at 2 mm, $d^{20}_4$ 1.0498, $n^{20}D$ 1.4454 (according to data [3]: b.p. 100° at 2 mm); $MR_D$ 35.2, calc. 35.4.

Found %: N 9.46, 9.67. $C_7H_9O_2N$. Calculated %: N 10.00.

5. p-Cyanophenyl methacrylate. To a mixture of 6 g of p-cyanophenol, 8 g of sodium carbonate, 0.5 g of cuprous chloride, 25 g of isopropyl ether, there was added with energetic stirring over 15 minutes 6.5 g of methacrylyl chloride. Then the mixture was heated for four hours at 65°, allowed to settle and was filtered. The ethereal solution was washed with water until it became colorless and was then dried over calcium chloride. After evaporation of the ether in vacuum there was obtained 3.3 g of p-cyanophenyl methacrylate (yield 35% based on the phenol); needles from ethyl alcohol (1.8 g) with m.p. 82-83°.

Found %: C 71.72, 71.92; H 5.70, 6.11; N 7.15, 7.26. $C_{11}H_9O_2N$. Calculated %: C 70.6; H 4.8; N 7.4.

p-Cyanophenol was prepared by a modified method of Sandmeyer, used for the preparation of 2-fluoro-4--cyanophenol [9]. From 39 g of p-aminophenol there was obtained 19 g of crystalline p-cyanophenol. For its purification, the product was distilled twice in vacuum (b.p. 161-162° at 6 mm). The distilled p-cyanophenol (14.8 g) had m.p. 113°.

**6. Methacrylamidoacetonitrile.** To a mixture of 29 g of aminoacetonitrile [10] and 116 g of dry acetone there was added at 0-3° with stirring 27 g of methacrylyl chloride, after which the mixture was stirred at room temperature for half an hour longer. The precipitated hydrochloride of aminoacetonitrile was filtered off and washed with dry acetone.

The crystalline product remaining after evaporation of acetone was subjected to a vacuum distillation after addition of cuprous chloride. There was obtained 17 g of methacrylamidoacetonitrile with b.p. 165-167° at 3 mm and m.p. 32-34°. The yield was 53% based on the chloride.

Found %: C 58.5, 58.1; H 6.4, 6.6; N 21.9, 21.6. $C_6H_8ON_2$. Calculated %: C 58.1; H 6.4; N 22.5.

**7. Vinylidene cyanide.*** For the preparation of 1,1,3,3-tetracyanopropane, 50 g of freshly distilled malononitrile was dissolved in 250 ml of ethyl alcohol and to the resulting solution was added 29 g of 40% solution of formaldehyde. The mixture was allowed to stand at room temperature for one day or two days depending on the rate of precipitation of crystals. Then the crystals were filtered off, washed with N solution of sulfuric acid, wtih water and alcohol, and were dried in air. The final drying of the crystals was done in vacuum of 5 mm at 100-105°. The yield was 47.5 g (52.6%); the substance melts at 130-135° to a transparent fluid.

The thus prepared 1,1,3,3-tetracyanopropane was subjected to pyrolysis without further purification. The pyrolysis of 1,1,3,3-tetracyanopropane was run in the presence of phosphorus pentoxide at 180-185° at 15 mm. A Wurtz flask with a wide take-off tube, hich was bent and connected to a receiver which was cooled with ice and salt, was used for the pyrolysis. The vacuum pump was connected to the receiver through a calcium chloride tube. The flask with the original 1,1,3,3-tetracyanopropane was heated on an oil bath at 180-185° and maintained at this temperature and 15 mm pressure for two hours. A small amount of phosphorus pentoxide was placed into the receiver, the take-off tube and among the starting 1,1,3,3-tetracyanopropane crystals. From 10 g of the charged 1,1,3,3-tetracyanopropane there was obtained 8-9 g of the pyrolysis products. After distillation of the pyrolyzate there collected in the receiver some 5 g of a fraction which boiled up to 70° at 10 mm. After two distillations of this fraction there was obtained 4 g of vinylidene cyanide with b.p. 50° at 10 mm (according to data [5], b.p. 50.5° at 10 mm).

**8. Methyl α-cyanoacrylate.** a) To 112 ml of anhydrous methanol there was added with stirring 9 g of finely cut metallic sodium, followed by 40 g of methyl cyanoacetate. The mixture was heated for 1.5 hours on a boiling water bath. The, at the temperature of from −5° to + 2° and with stirring, there was added a mixture of 46 g of chloromethyl acetate [11] and 12 ml of anhydrous methanol, after which the stirring was continued for half an hour at room temperature.

Methyl alcohol was distilled in vacuum and the remaining residue was shaken for two hours with 280 ml of water. The aqueous layer was separated and the semisolid residue was dissolved in acetone. The solution was dried with sodium sulfate and acetone was distilled in vacuum. To the residue there was added 1-2 g of phosphorus pentoxide, after which the product was subjected to a vacuum distillation, for which a small amount of phosphorus pentoxide was placed in the condenser and the receiver.

There was obtained 8.6 g (19.2% calculated on the initial methyl cyanoacetate) of methyl α-cyanoacrylate.

B. p. 47-48° at 2 mm, $d^{20}_4$ 1.1012, $n^{20}D$ 1.4430. $MR_D$ 26.72; calculated 26.24.

Found %: C 53.22, 53.40; H 4.57, 4.92; N 12.74; 12.57. $C_5H_5O_2N$. Calculated %: C 54.05; H 4.50; N 12.6.

b) To 20.5 g of 37% solution of formaldehyde there was added 3 drops of piperidine after which 28 g of methyl cyanoacetate was added at 20-40° with stirring. The mixture was stirred at 80° for one hour longer.

After cooling, the aqueous layer was separated and the polymerized product was dissolved in acetone and worked up as in experiment a. There was obtained 12.3 g (39% on methyl cyanoacetate) of methyl α-cyanoacrylate with b.p. 46-47° at 1 mm, $n^{20}D$ 1.4430.

## SUMMARY

A detailed description is given for the methods of synthesis and the properties of α-cyanoethyl methacrylate,

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* Done by I. N. Beliaeva.

**β-cyanoethyl methacrylate, α-cyanoisopropyl methacrylate, α-cyanobenzyl methacrylate, p-cyanophenyl methacrylate, methacrylamidoacetonitrile, vinylidene cyanide and methyl α-cyanoacrylate, of which α-cyanoethyl methacrylate, α-cyanobenzyl methacrylate, p-cyanophenyl methacrylate and methacrylamidoacetonitrile were prepared and described for the first time.**

## LITERATURE CITED

[1] D. T. Mawry, J. Am. Chem. Soc., 66, 371 (1944).

[2] C. S. Marvel and W. S. Anderson, Ind. Eng. Chem., 47, 344 (1955).

[3] U.S. Patent 2379297; Chem. Abstr. 39, 5128 (1945).

[4] N. N. Lebedev and L. V. Andrianova, J. Gen. Chem. 25, 210 (1955).*

[5] A. E. Ardis, S. J. Averill, J. Am. Chem. Soc., 72, 1305, (1950), U.S. Patent 2514387; Chem. Abstr. 45, 639 (1951).

[6] O. Diels and H. Gärtner, Ber., 55, 3439 (1922).

[7] U.S. Patent 2467926, 2467927; Chem. Abstr. 43, 6222 (1949).

[8] A. I. Ultee, Rec. trav. chim., 28, 1 (1909).

[9] S. S. Berg, G. Newbery, J. Chem. Soc., 1949, 643.

[10] G. A. Menge, J. Am. Chem. Soc., 56, 2197 (1934).

[11] I. M. Descud'e, Bull, Soc. Chim. (3) 27, 867 (1902).

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# REACTION OF NITROGEN TETROXIDE WITH ORGANIC COMPOUNDS

## I. A STUDY OF CONDITIONS OF REACTION OF NITROGEN TETROXIDE WITH BENZALDOXIME. COMPOSITION OF PRODUCTS AND REACTION EQUATION.

S. S. Novikov, L. I. Khmel'nitskii and O. V. Lebedev

The reaction of nitrogen tetroxide with aromatic aldoximes, discovered by Ponzio in 1906 [1], is to this day one of the important methods of introduction of two nitro groups into a methyl side chain of various aromatic compounds [2-5].

$$ArCH{=}NOH \xrightarrow{N_2O_4} ArCH(NO_2)_2$$

It follows from Ponzio's work that an excess of nitrogen tetroxide has a material significance in the reaction. At molar ratio of nitrogen tetroxide and benzaldoxime of 1 : 1 there occurs a considerable development of the side reactions with formation of benzaldoxime peroxide, 3,4-diphenylfuroxane (so-called diphenylglyoxime peroxide) and benzaldehyde; phenyldinitromethane is formed in a 33% yield. With double amount of nitrogen tetroxide the yield of phenyldinitromethane is raised to 49.5% and only benzaldehyde is formed amoung the byproducts.* If one takes 0.5 mole of nitrogen tetroxide per 1 mole of aldoxime, the reaction proceeds in the direction of formation of nitrolic acid [4].

The degree of development of side reactions depends also on the structure of the aldoximes themselves. For example, anisaldoxime and piperonaldoxime give good yields of the corresponding gem-dinitro derivatives with only equimolar amount of nitrogen tetroxide, while only aldehydes are formed among the byproducts [2, 3]. On the other hand, o-, p-nitro- and o,p-dinitrobenzaldoximes yield the corresponding nitroaryldinitromethanes in but negligible amounts [5].

We decided to study systematically the reaction of nitrogen tetroxide with benzaldoxime. We studied the effect of the molar ratio, concentration and the mode of mixing the reactants, as well as the nature of the solvent, on the course of the reaction.

Among all the solvents used by us, except ether and dioxane, the maximum yield of phenyldinitromethane was reached at the molar ratio of reactants that was close to unity (Fig. 1). In case of ether, the maximum is shifted toward the double amount of nitrogen tetroxide, which fact agrees with Ponzio's observations. In running the reaction in dioxane one reaches high yields at the molar ratio of nitrogen tetroxide to benzaldoxime of 4 : 1 and higher.

This shift of the maximum yield of phenyldinitromethane is explained evidently by the fact that both ether and dioxane react with nitrogen tetroxide forming complexes $N_2O_4 \cdot 2(C_2H_5)_2O$ and $N_2O_4 \cdot O(CH_2CH_2)_2O$ [6].

The yield of phenyldinitromethane drops sharply after a decrease of the optimum amount of nitrogen tetroxide: thus at only 0.5 mole of nitrogen tetroxide per 1 mole of the oxime, phenyldinitromethane is practically not formed at all and much 3,4-diphenylfuroxane is obtained.

The maximum yield of phenyldinitromethane (about 43%) is attained with concentrations of about 5 g of the oxime per 100 ml of the solvent (ether or benzene). At higher concentrations the yield declines noticeably, but it is changed but little by further dilution (Fig. 2).

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* In Ponzio's papers all the indicated yields were calculated incorrectly (too high values are given). Here we supply the corrected figures.

The yield of phenyldinitromethane also depends on the nature of the solvent, which fact is evident in Fig. 1.

With excess of nitrogen tetroxide over the optimum amount, the yield of phenyldinitromethane is lowered slightly in ether and dioxane. In other solvents, for example in carbon tetrachloride, the harmful effect of excess nitrogen tetroxide on the yield of phenyldinitromethane can be weakened noticeably by dilution (see curves 2 and 11 in Fig. 1).

Benzaldehyde is formed almost exclusively (88-93%) if the reaction is run in the absence of a solvent. The solvent must be dry, since in the presence of water there occurs the development of side reactions, mainly the formation of 3,4-diphenylfuroxane. The order and the method of mixing of the reactants also produce a material effect on the yield of phenyldinitromethane. It is best to pour the entire amount of nitrogen tetroxide into the oxime solution in one portion.

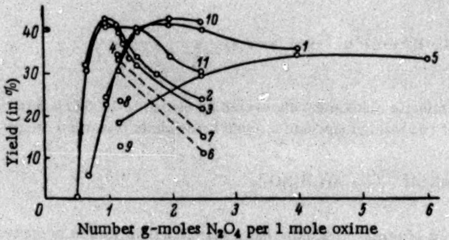

Fig. 1. Ratio of reactants in various solvents (curves 1-9 correspond to 5 g of oxime in 50 ml of solvent, 10 and 11 to 5 g of oxime in 100 ml of solvent): in ether (1), carbon tetrachloride (2), benzene (3), chlorobenzene (4), dioxane (5), chloroform (6), petroleum ether (b.p. 45-55°) (7), 1,2-dichloroethane (8), nitrobenzene (9), ether (10), and carbon tetrachloride (11).

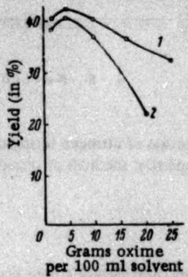

Fig. 2. Curves of dependence of yields of phenyldinitromethane on concentration of reactants in ether (1) and in benzene (2), with molar ratio of nitrogen tetroxide and benzaldoxime being 2 : 1 in ether and 1.2 : 1 in benzene.

Thus, it appeared that it is possible to raise the yield of phenyldinitromethane in the reaction of nitrogen tetroxide with benzaldoxime, with ice cooling, only to 43% by alteration of the proportion, the concentration and the mode of mixing of the reactants, as well as by alteration of the nature of the solvent.*

We decided to establish the qualitative and the quantitative composition of all reaction products and the variation of this composition in its dependence on the ratio of reactants and the presence of a solvent, in order to study this reaction more exhaustively.

The results of the experiments are shown in Table 1 and are summarized thus.**

1. With molar ratio of nitrogen tetroxide and benzaldoxime close to unity and greater than unity, the reaction in a solvent proceeds with formation of only phenyldinitromethane and benzaldehyde (total yield of 97%).

2. With molar ratio of reactants being 0.5 : 1, the reaction in a solvent proceeds mainly with the formation of 3,4-diphenylfuroxane (46%) and only to an insignificant degree with formation of phenyldinitromethane (4%) and benzaldehyde (9%).

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* The yield of 49.5%, which was obtained in running the reaction in ether [1], was attained also by us if we treated the ethereal solution according to Ponzio, i.e., with a solution of base. However, the product obtained in this manner contained noticeable amounts of admixtures and melted at 65-70°, while after the extraction of phenyldinitromethane from the reaction mixture with bicarbonate solution the product is obtained directly in very pure state with m.p. 78°.

** Each experiment was repeated 2-3 times. In Table 1 there are given the mean values from each series of experiments.

3. In running the reaction without a solvent one forms the aldehyde almost quantitatively (93%).

4. The gaseous reaction products consist practically only of nitrogen and NO, in addition to the unreacted nitrogen tetroxide.

One of the important new results of our experiments, in comparison with the previous work, is the establishment of the fact that some nitrogen is evolved in the reaction of nitrogen tetroxide with benzaldoxime.

TABLE 1

Composition of Reaction Products of $N_2O_4$ with Benzaldoxime (in grams)

| No. of exp. | Taken, number of grams of $N_2O_4$ for the reaction with 5.00 g of benzaldoxime | $CCl_4$ (in ml) | Reaction products* | | | | $N_2O_4$ | |
|---|---|---|---|---|---|---|---|---|
| | | | $N_2$ | NO | $C_6H_5CH(NO_2)_2$ | $C_6H_5CHO$ | unreacted | reacted |
| 1 | 4.59 | 50 | 0.32 | 1.29 | 2.47 | 2.80 | 0.88 | 3.71 |
| 2 | 8.87 | 50 | 0.30 | 2.12 | 1.57 | 3.35 | 2.50 | 6.33 |
| 3** | 1.94 | 50 | 0.22 | 0.11 | 0.31 | 0.40 | 0 | 1.94 |
| 4 | 3.98 | Without solvent | 0.18 | 1.97 | 0 | 3.20 | 0.33 | 3.65 |
| 5 | 9.02 | Ditto | 0.16 | 2.67 | 0.10 | 4.10 | 2.49 | 6.53 |

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* In addition to this, in all experiments there was formed about 2.6 g of nitric acid (1 mole per 1 mole of benzaldoxime).

** In experiment 3, in addition to the listed reaction products, there was formed 2.22 g of 3,4-diphenylfuroxane (0.23 mole per mole of oxime) and 0.21 g of white powder and 1.7 g of an oil, whose nature was unknown.

The data from our experiments (Table 1) permit us to set up the equations which reflect the final results of the reaction both in the direction of formation of phenyldinitromethane and in the direction of formation of benzaldehyde.

$$4C_6H_5CH{=}NOH + 7N_2O_4 = 4C_6H_5CH(NO_2)_2 + 4HNO_3 + 4NO + N_2 \qquad (1)$$

$$4C_6H_5CH{=}NOH + 5N_2O_4 = 4C_6H_5CHO + 4HNO_3 + 8NO + N_2 \qquad (2)$$

The following considerations lie in the formulation of these equations.

1. From each molecule of benzaldoxime there is formed either a molecule of phenyldinitromethane or a molecule of benzaldehyde, since their combined yield is not under 97% (Experiments 1 and 2).

2. Nitrogen is evolved during the reaction in a rather constant amount: in experiments 1-3 there was formed 0.19-0.28 moles per 1 mole of the original oxime, i.e., about 0.25 mole. Hence we obtained the corresponding coefficient for nitrogen in both equations.

3. In experiment 5 the reaction proceeded almost completely to form benzaldehyde; the yield was 93% (yield of phenyldinitromethane was 1%). There was evolved 2 moles of NO per 1 mole of aldehyde, or what is the same thing, per 1 mole of the original oxime. From this we obtained the coefficient for NO for Equation (2).

In Experiment 2 there was formed, per 1 mole of oxime, 0.76 mole of aldehyde, which, according to Equation (2) should be accompanied by the evolution of 0.76 · 2 = 1.52 moles of NO. There was actually evolved 1.71 moles of NO, i.e., with excess of 0.19 mole. This excess must be evidently related to the reaction of formation of phenyldinitromethane, which was isolated in the amount of 0.21 mole. Consequently, per 1 mole of the formed phenyldinitromethane there is evolved 1 mole of NO. Hence we obtained the coefficient for NO for Equation (1).

4. The hydrogen atom of the oxime group should be, in both cases, taking part in the formation of the molecule of nitric acid since the other possible inorganic products ($H_2O$ and $HNO_2$) formed with its participation, will in the final result pass into nitric acid. Then per 1 mole of the oxime there should form 1 mole of nitric acid.

We proved the presence of nitric acid in the reaction mixture in a qualitative manner. The quantitative determination of nitric acid in the presence of residues of unreacted nitrogen tetroxide is difficult.

An indirect confirmation of the direct formation of nitric acid is the reaction of nitrogen tetroxide with the sodium salt of benzaldoxime which also leads to the formation of phenyldinitromethane, while sodium nitrate is formed in 95% yield, with an insignificant admixture of sodium nitrite (a weak qualitative test). If sodium nitrite were the primary reaction product, it would not have changed further under the action of nitrogen tetroxide (the stability of sodium nitrite in respect to nitrogen tetroxide was established by a separate experiment).

The correctness of the deduced equations is confirmed also by Experiment 4. In this experiment nitrogen tetroxide was taken in smaller amount than required by Equation (2); this explains the lowered yield of benzaldehyde (73%). In calculation with Equation (2) this amount of aldehyde corresponds to 0.93 mole of reacted nitrogen tetroxide, 0.18 mole of evolved nitrogen and 1.46 moles of evolved NO. According to data from Experiment 4, there took part in the reaction 0.96 mole of nitrogen tetroxide and there was evolved 0.16 mole of nitrogen and 1.59 moles of NO.

Let us consider the other attempts, described in the literature, to explain the course of the reaction of nitrogen tetroxide with benzaldoxime.

Fieser and Doering [5] in 1946 proposed an equation for the formation of phenyldinitromethane which failed to consider the reaction of water with excess nitrogen tetroxide and which did not reflect the fact of evolution of nitrogen. A. I. Titov in constructing the scheme for the course of this reaction started with the radical mechanism of nitration of hydrocarbons by nitrogen oxides, developed by him [7, 8]. The scheme of A. I. Titov does explain the formation of phenyldinitromethane, but does not explain that of benzaldehyde.

Besides this, the oxime group is replaced by two nitro groups by the action of nitrogen tetroxide not only in aldoximes but also in ketoximes of the aromatic series, which fact is difficult to explain by Titov's scheme since there is no hydrogen in such ketoximes — the hydrogen which by cleavage could form a radical which lies in the origination of the dinitro derivative in this reaction scheme. Finally in Titov's scheme there is the absence of free nitrogen, whose formation has been accounted for in our experiments.

Our data are still insufficient to make a definite conclusion about the reaction mechanism. However the fact that nitrogen is evolved in a rather constant amount under different conditions of the experiments (Table 1, Experiments 1-3) permits us to suppose that the reaction begins at the same stage which is accompanied by evolution of nitrogen. After this stage there are developed the secondary reactions which lead to the formation of the various end products, depending on the experimental conditions.

## EXPERIMENTAL

The commercial nitrogen tetroxide was purified by distillation from phosphoric anhydride in a stream of oxygen. Benzaldoxime was prepared from benzaldehyde and hydroxylamine according to Beckmann [9]. We took 5 or 20 g of benzaldoxime for all experiments, using dry solvents.

Action of nitrogen tetroxide on benzaldoxime in a solvent. To an ice-cooled solution of benzaldoxime in an organic solvent there was added liquid nitrogen tetroxide, all at once. The solution turned green after one minute and began to evolve gas bubbles. The solution foamed and warmed up noticeably. The reaction was completed after a few minutes and the color of the reaction mixture became brown. Then* the reaction mixture was washed twice with water and treated several times with 10% solution of sodium bicarbonate. From the bicarbonate extracts we precipitated the phenyldinitromethane by means of 10% sulfuric acid. The precipitate was filtered off by suction and the solid was washed with water and then dried in air.

After the isolation of phenyldinitromethane the reaction mixture was shaken with an alkaline solution of hydroxylamine and the benzaldehyde was converted to the oxime, passing into the aqueous layer in the form of its sodium salt. The latter was decomposed with carbon dioxide, the oxime was extracted with carbon tetrachloride, the extract was dried with anhydrous sodium sulfate and evaporated at room temperature; the residual oxime was weighed.

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* Ponzio, after completion of the reaction, kept the reaction mixture for one hour at room temperature; however, our experiments showed that the yield is not decreased by omission of the holding period.

In the experiment run with 0.5 mole of nitrogen tetroxide per 1 mole of benzaldoxime, there formed a precipitate. After washing this precipitate with alkali, the insoluble portion was identified by mixed melting point with authentic benzaldoxime peroxide (m.p. 105°). After extraction of phenyldinitromethane and benzaldehyde, the reaction mixture was washed with water, dried with anhydrous sodium sulfate and evaporated in the cold. The resulting crystals were those of 3,4-diphenylfuroxane: m.p. 115° (from alcohol); yield – 45.3% (according to [1], m.p. 115°).

Found %: C 70.40, 70.26; H 4.31, 4.32; N 11.94, 11.84. $C_{14}H_{10}O_2N_2$. Calculated %: C 70.58; H 4.23; N 11.76.

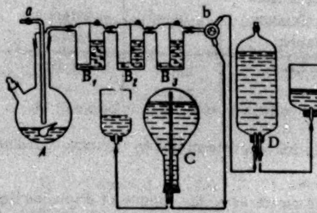

Fig. 3. Apparatus for collection of gaseous products of the reaction of nitrogen tetroxide with benzaldoxime.
A) Reaction flask; $B_1$, $B_2$, $B_3$) absorbers with 50% solution of potassium iodide; C) gasometer with a strong solution of table salt; D) absorber with 50% solution of potassium hydroxide; a) a cock for admission of carbon dioxide; b) a three-way stopcock.

Action of nitrogen tetroxide on benzaldoxime without a solvent. Three and a half g of benzaldoxime cooled with ice and salt to −10° was added with stirring, dropwise, to 6.6 g of nitrogen tetroxide (2.5 moles of nitrogen tetroxide per 1 mole of oxime). The reaction was accompanied by an energetic evolution of nitrogen oxides and heat.

Then the green mixture was treated with water and a solution of sodium carbonate. The oily layer was separated and distilled. There was obtained 2.7 g of benzaldehyde with b.p. 178-179°. The yield was 88%. Benzaldehyde phenylhydrazone, m.p. 158°. The mixed melting point with authentic benzaldehyde phenylhydrazone gave no depression.

The quantitative determination of benzaldehyde was run by treatment of the reaction mixture with alkaline solution of hydroxylamine with a subsequent isolation of the oxime by means of a stream of carbon dioxide.

Action of nitrogen tetroxide on sodium salt of benzaldoxime. Sodium salt of benzaldoxime was prepared by the action of sodium ethoxide on benzaldoxime in a mixture of alcohol and petroleum ether; the product was dried at 100° in vacuum in an air stream which was freed of moisture and carbon dioxide. The yield was 60%.

Found %: Na 16.0. $C_7H_6ONNa$. Calculated %: Na 16.07.

To a suspension of 5.9 g of sodium salt of benzaldoxime in 50 ml of dry carbon tetrachloride, cooled with ice, there was added with stirring 7.6 g of nitrogen tetroxide (2 moles of nitrogen tetroxide per mole of the salt). A vigorous evolution of gases took place and a mild heat evolution.

The precipitate was filtered off, washed with carbon tetrachloride and dried. The qualitative test for the nitrite ion (with 2-naphthol and sulfanilic acid) was very weak while that for the nitrate ion (with diphenylamine) was positive. The yield of sodium nitrate was 3.30 g (95%).

Found %: Na 26.9, 27.0. $NaNO_3$. Calculated %: Na 27.05.

The filtrate was washed with water and extracted with 10% solution of sodium bicarbonate. By acidification of the extract with 10% sulfuric acid there was isolated 1.79 g (24%) of phenyldinitromethane with m.p. 78°.

Analysis of gases. For collection and study of all the reaction products, the operations were performed in a closed flask with an outlet tube through which the gases were led into a system of absorbers and were collected in a gasometer. The scheme of the apparatus is shown in Fig. 3.

A 50% solution of potassium iodide is placed in absorbers $B_1$, $B_2$ and $B_3$ for absorption of nitrogen dioxide.

The gasometer C with a strong solution of table salt serves for the collection of the gases which are not retained in the absorbers $B_1$, $B_2$ and $B_3$; into the gasometer also passes the carbon dioxide in the stream of which the experiment is being run. The absorber D with a 50% solution of potassium hydroxide serves for the absorption of carbon dioxide.

In the reaction flask A there was placed a solution of a sample of benzaldoxime in 50 ml of carbon tetrachloride and a thin-walled ampul with a sample of nitrogen tetroxide.*

The entire system was filled with carbon dioxide, dried over concentrated sulfuric acid and phosphoric anhydride, after which the ampul was broken. The gases passing through absorbers $B_1$, $B_2$, and $B_3$ were collected in gasometer C. After completion of the reaction the entire system was again flushed with a stream of carbon dioxide until the solution in flask A became light yellow, while the gas mixture was collected in the absorber D.

TABLE 2

| Name of gas | Time of flow of the gas (in seconds) | Density relative to air | | Molecular weight | |
|---|---|---|---|---|---|
| | | found | data from reference tables | found | data from reference tables |
| Nitrogen . . . . . . . . . . . . . . . . . | 69.90 | 0.978 | 0.967 | 28.37 | 28.016 |
| Gas being studied . . . . . . . . . . | 72.75 | 1.082 | – | 31.39 | – |

The amount of nitrogen tetroxide which failed to enter the reaction was determined by titration of iodine separated in absorbers $B_1$, $B_2$, and $B_3$ with thiosulfate [10].

The gas from absorber D was transferred into the gasometer and measured by the volume of displaced liquid. Brown nitrogen dioxide formed on release of the gas into the atmosphere; consequently, NO was contained in the gas. The quantitative determination of NO in the gas mixture was performed in a gas burette with acidified solution of ferrous sulfate.

A large volume of gas, which was composed of nitrogen, always remained after the absorption of NO. A glowing splinter was immediately extinguished in it. After analysis of the gas in Orsat apparatus, the unabsorbed residue amounted to 92%. After the determination of gas density by the method of flow through a narrow opening in a Schilling apparatus [11] and then after the calculation of the molecular weight from the density, there were obtained the results which are shown in Table 2.

As it is clearly evident from the data in the table, the gas density is very close to that of nitrogen. With slow passage of the gas through a vessel immersed in liquid nitrogen, the gas failed to be condensed. It was natural to suppose that some nitrous oxide could be present in the gas under examination since this substance is rather readily soluble in alcohol; however, the gas volume failed to change after washing with alcohol.

Benzaldehyde and phenyldinitromethane were quantitatively determined in the reaction mixture after the completion of gas analysis.

It is possible to judge the presence of nitric acid in the reaction mixture by the results of the following experiment. The reaction mixture was blown with dry carbon dioxide, after the completion of the reaction, to freeing it from nitrogen oxides and after that it was shaken with a large volume of water. The acidity of the medium was determined in the aqueous extract (by titration with alkali in the presence of phenolphthalein) while the amount of nitrous acid was determined iodometrically. It turned out that the acidity of the aqueous extract was some ten times greater than the acidity caused by the presence of nitrous acid. This acidity could not be caused by an organic acid since the sole organic reaction products were phenyldinitromethane and benzaldehyde. Thus, the presence of only nitric acid, of the inorganic acids, could be allowed.

In a blank experiment in dry carbon tetrachloride we dissolved 1 g of nitrogen tetroxide and the solution was blown with carbon dioxide and thoroughly shaken with a large volume of water. The same amount of nitrous acid was found in the aqueous extract as was found in the previous experiment, i.e., this acid formed by hydrolysis of traces of nitrogen oxides remaining in the solvent. The acidity of the aqueous extract exceeded the acidity caused by the presence of nitrous acid by a factor of two, which is just correct for the hydrolysis equation: $N_2O_4 + H_2O \rightarrow HNO_3 + HNO_2$.

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* In case of running the reaction without a solvent, there was placed a sample of benzaldoxime in the vessel. A, while liquid nitrogen tetroxide was introduced from a dropping funnel through a side-neck.

## SUMMARY

1. The effect of molar proportions, concentration and mode of mixing of reactants, as well as the nature of the solvent, was studied in respect to the course of the reaction of nitrogen tetroxide with benzaldoxime, with ice cooling.

2. The yield of phenyldinitromethane cannot rise over 43% owing to the effects of the factors listed above.

3. The qualitative and the quantitative compositions of all reaction products of $N_2O_4$ and benzaldoxime, run under various conditions, were determined.

4. Evolution of nitrogen in the course of this reaction was detected.

5. Equations which describe the formation of phenyldinitromethane and benzaldehyde in this reaction were proposed.

6. Phenyldinitromethane was prepared by the action of nitrogen tetroxide on the sodium salt of benzaldoxime.

## LITERATURE CITED

[1] G. Ponzio, J. pr., Ch., 73 (2), 494 (1906); Gazz., 36, 287 (1906).

[2] G. Ponzio, Gazz., 36, 588 (1906).

[3] G. Ponzio, Atti Lincei, 15 (5), 42, 118 (1906).

[4] G. Ruggeri, Atti Accad. Scienze Torino, 58, 441 (1923); Gazz., 53, 691 (1923).

[5] L. Fieser and W. Doering, J. Am. Chem. Soc., 68, 2252 (1946).

[6] H. Ling and H. Sisler, J. Am. Chem. Soc., 75, 5191 (1953).

[7] A. I. Titov, J. Gen. Chem. 18, 465 (1948).

[8] A. I. Titov, J. Gen. Chem. 7, 1695 (1937).

[9] E. Beckmann, Ber., 23, 1684 (1890).

[10] F. Raschig and W. Prahl, Z. ang. Ch., 42, 253 (1929).

[11] A. P. Lidov, Analysis of gases, Kharkov; p. 277 (1907).[in Russian].

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# REACTION OF NITROGEN TETROXIDE WITH ORGANIC COMPOUNDS

## II. REACTION OF NITROGEN TETROXIDE WITH ACI-PHENYLNITROMETHANE AND ITS SALT

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During the study of the reaction of nitrogen tetroxide with benzaldoxime and its salt, a reaction leading to phenyldinitromethane, we were obliged to study the reaction of nitrogen tetroxide with aci-phenylnitromethane and its salt. It is mentioned in the literature that "the aci-form of phenylnitromethane enters rather readily into a reaction with nitrogen dioxide" [1], but no data are cited. Experiments set up by us showed that, as should have been expected, from analogy with other alkaromatic nitro compounds [1], the acid-form of phenylnitromethane and its salt yields phenyldinitromethane in reaction with nitrogen tetroxide.

$$C_6H_5CH{=}NOONa \xrightarrow{N_2O_4} C_6H_5CH(NO_2)_2 \xleftarrow{N_2O_4} C_6H_5CH{=}NOOH$$

The maximum yield of phenyldinitromethane from aci-phenylnitromethane was 44.5%, while the yield from the salt of phenylnitromethane was 28%.

The reaction was run in a solvent and in its external appearance resembled greatly the reaction of nitrogen tetroxide with benzaldoxime and its salt, but evidently proceeded with considerably smaller heat evolution.

### EXPERIMENTAL

The sodium salt of phenylnitromethane was prepared by Titov's method [2]. Aci-phenylnitromethane (m.p. 84°) was prepared by acidification of a solution of the sodium salt of phenylnitromethane with 10% sulfuric acid.

*Reaction of nitrogen tetroxide with aci-phenylnitromethane.* To 0.68 g of aci-phenylnitromethane in 10 ml of dry ether, cooled with ice, there was added 0.45 g of nitrogen tetroxide and the cooling was stopped. The solution became bright green, gas bubbles formed and a colorless precipitate appeared.

After ten minutes' standing, the precipitate was filtered off and washed three times with dry ether. There was obtained 0.10 g of a substance with m.p. 68°. The structure of this substance was not determined.

The ethereal solution was shaken with a saturated solution of sodium bicarbonate. Phenyldinitromethane was precipitated from the bicarbonate extract by acidification with 10% sulfuric acid, filtered off, washed with water and dried in air. There was obtained 0.20 g of phenyldinitromethane (22%); m.p. 77°. A mixed melting point with authentic phenyldinitromethane gave no depression.

With a large excess of nitrogen tetroxide (3.6 g), while running the reaction without cooling, the substance with m.p. 68° failed to form.

The results and the conditions of running the experiments with aci-phenylnitromethane are collected in Table 1.

*Reaction of nitrogen tetroxide with sodium salt of phenylnitromethane.* Into a suspension of 1 g of sodium salt of phenylnitromethane in 28 ml of dry ether there was added in one portion 1.2 g of nitrogen tetroxide dissolved in 2 ml of dry ether. The reaction mixture turned green and gas bubbles began to appear. A mild heat evolution occurred. After 20-30 seconds the mixture turned orange.

## TABLE 1

Reaction of Nitrogen Tetroxide With aci-Phenylnitromethane (in 10 ml of ether)

| Taken, $N_2O_4$ (in g) for the reaction with 0.68 g of $C_6H_5CH =$ $= NOOH$ | Molar ratio of $N_2O_4 : C_6H_5CH = NOOH$ | Initial temperature of the mixture | Yield of phenyldinitromethane (in %) |
|---|---|---|---|
| 0.45 | 1 : 1 | 0° | 22 |
| 0.9 | 2 : 1 | 0 | 31 |
| 1.8 | 4 : 1 | 0 | 33.5 |
| 3.6 | 8 : 1 | 0 | 33.5 |
| 1.8 | 4 : 1 | 20 | 44.5 |

## TABLE 2

Reaction of Nitrogen Tetroxide with Salt of Phenylnitromethane.

| Taken, $N_2O_4$ (in g) for reaction with 1 g of $C_6H_5CH =$ $= NOONa$ | Molar ratio of $N_2O_4 : C_6H_5CH =$ $= NOONa$ | Solvent (30 ml) | Initial temperature of the mixture | Yield of phenyldinitromethane (in %) |
|---|---|---|---|---|
| 0.6 | 1 : 1 | Ether | 20° | 16.5 |
| 1.2 | 1 : 2 | Ether | 20 | 27.0 |
| 2.4 | 1 : 4 | Ether | 20 | 28.0 |
| 2.4 | 1 : 4 | Dichloroethane | 20 | 16.5 |
| 2.4 | 1 : 4 | Dichloroethane | 40 | 12.0 |
| 2.4 | 1 : 4 | Dichloroethane | 70 | 11.5 |

Sodium nitrate was filtered off (positive test for nitrate ion and negative test for nitrite ion). The filtrate was treated as in the experiments with aci-phenylnitromethane. The yield of phenyldinitromethane was 0.31 g (27%); m.p. 78°.

The results and the conditions of running the experiments with the sodium salt of phenylnitromethane are given in Table 2.

It is evident from the results of experiments run in dichloroethane that with elevation of the initial temperature of the reaction mixture the yield of phenyldinitromethane declines.

## SUMMARY

In the reaction of nitrogen tetroxide with aci-phenylnitromethane and its sodium salt there is formed phenyldinitromethane in yields of 44.5% and 28% respectively.

## LITERATURE CITED

[1] A. I. Titov and V. V. Smirnov, Doklady Akad. Nauk SSSR 83, 243 (1952).

[2] A. I. Titov, J. Gen. Chem. 10, 1881 (1940); 18, 475 (1948).

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# REACTION OF NITROGEN TETROXIDE WITH ORGANIC COMPOUNDS

## III. REACTION OF NITROGEN TETROXIDE WITH SALTS OF ALIPHATIC NITRO COMPOUNDS

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It is known that dinitro compounds are formed in the reaction of nitrogen tetroxide with aromatic oximes and with salts of arylnitromethanes. For example, benzophenone oxime [1] and the salt of diphenylnitromethane [2] yield diphenyldinitromethane, $(C_6H_5)_2C(NO_2)_2$, with nitrogen tetroxide.

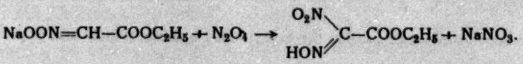
Aliphatic oximes form nitroso nitro compounds in the reaction with nitrogen tetroxide: for example, acetoxime yields propylpseudonitrole with nitrogen tetroxide [3]; the product has the formula $(CH_3)_2C(NO)(NO_2)$. By analogy with the generality of reactions of oximes and nitro compounds of the aromatic series one should expect a similar generality for the aliphatic series as well, i.e., the salts of aliphatic nitro compounds would yield nitroso nitro compounds with nitrogen tetroxide.

The possibility of reactions of this type was confirmed in the present work with examples of alkaline salts of 2-nitropropane, ethyl ester of nitroacetic acid and 1,1-dinitroethane.

Thus, in the reaction of sodium salt of 2-nitropropane with nitrogen tetroxide there was formed propylpseudonitrole:

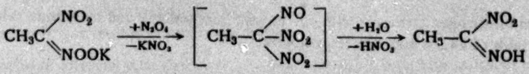
$$(CH_3)_2C{=}NOONa \xrightarrow{N_2O_4} (CH_3)_2C(NO)(NO_2) + NaNO_3.$$

In the reaction of sodium salt of nitroacetic ester with nitrogen tetroxide there was formed the ethyl ester of nitro-oximinoacetic acid.



$$NaOON{=}CH{-}COOC_2H_5 + N_2O_4 \longrightarrow \overset{O_2N}{\underset{HON}{\phantom{x}}}\!\!>C{-}COOC_2H_5 + NaNO_3.$$

In the reaction of potassium salt of 1,1-dinitroethane with nitrogen tetroxide there was formed ethylnitrolic acid. In this case, evidently, an unstable nitroso compound formed first, then decomposed with formation of ethylnitrolic acid under the influence of moisture during the evaporation of the ethereal solution in an open vessel.



$$CH_3C\begin{smallmatrix}\nearrow NO_2\\ \searrow NOOK\end{smallmatrix} \xrightarrow[-KNO_3]{+N_2O_4} \left[CH_3{-}C\begin{smallmatrix}\nearrow NO\\ -NO_2\\ \searrow NO_2\end{smallmatrix}\right] \xrightarrow[-HNO_3]{+H_2O} CH_3{-}C\begin{smallmatrix}\nearrow NO_2\\ \searrow NOH\end{smallmatrix}$$

This is all the more probable since immediately on addition of nitrogen tetroxide the reaction mixture acquires an intensely blue color, which is characteristic of monomers of nitroso compounds, and which does not vanish until almost the very end of evaporation of the solution.

In the reaction of nitrogen tetroxide with the potassium salt of nitromalonic ester, contrary to expectations, there there was isolated only nitromalonic ester in a quantitative yield. As shown by a spectral study, the potassium salt of nitromalonic ester is formed not at the nitro group but at the carbonyl group: $C_2H_5OOCC(NO_2){=}C(OK)OC_2H_5$, which fact explains the anomalous course of the reaction.

## EXPERIMENTAL

*Reaction of nitrogen tetroxide with sodium salt of 2-nitropropane.* To a suspension of 1.11 g of sodium salt of 2-nitropropane in 30 ml of dry ether there was added 0.9 g of nitrogen tetroxide (1 mole per 1 mole of the salt) in 3 ml of dry ether. The reaction mixture turned green, warmed itself to 25-30° and evolved gas bubbles.

After completion of the reaction the inorganic salt was filtered off, washed twice with ether and dried. There was obtained 0.69 g of a mixture of sodium nitrate and nitrite (qualitative test).

The ethereal filtrate was evaporated at 20°. The residue was 0.12 g of a colorless crystalline substance with m.p. 72°, which waspropylpseudonitrole. After recrystallization from chloroform its m.p. was 75°. The mixed melting point withauthentic propylpseudonitrole (m.p. 76°) gave no depression.

An emerald green liquid formed after melting; solutions in carbon tetrachloride and chloroform had a blue color.

In the reaction of nitrogen tetroxide with the sodium salt of 2-nitropropane in 2 : 1 ratio we failed to form any propylpseudonitrole.

*Reaction of nitrogen tetroxide with sodium salt of ethyl ester of nitroacetic acid.* To a suspension of 0.5 g of sodium salt of nitroacetic ester in 10 ml of dry ether there was added 0.3 g of nitrogen tetroxide (1 mole per 1 mole of salt) in 2 ml of dry ether. The reaction proceeded analogously to the preceding one.

The ethereal solution, after its separation from the mixture of sodium nitrate andnitrite (0.28 g) was evaporated at 20°. In the residue there remained 0.43 g of crystals with a small admixture of an oil. The crystals were pressed dry, washed with 1 ml of chloroform, and purified by precipitation with heptane from chloroform, when they were shown to be those of the ethyl ester of nitro-oximinoacetic acid; m.p. 67.5-68°. According to data from [4]: m.p. 69°.

Found %: C 29.83, 29.85; H 3.66, 3.73; N 17.20, 17.30. $C_4H_6O_5N_2$. Calculated %: C 29.63; H 3.73; N 17.29.

*Reaction of nitrogen tetroxide with potassium salt of 1,1-dinitroethane.* To a suspension of 0.58 g of potassium salt of 1,1-dinitroethane in 10 ml of dry ether there was added 0.35 g of nitrogen tetroxide (1 mole per 1 mole of salt) in 2 ml of dry ether. The reaction mixture turned deep blue and warmed itself to 25-30°; no gases were evolved.

The ethereal solution was filtered from potassium nitrate (0.35 g; yield of 94.5%) and evaporated at 20°. After almost all the ether had evaporated, the reaction mixture began to decolorize rapidly and to crystallize. There was obtained 0.2 g (52.5%) of ethylnitrolic acid, which after precipitation from chloroform with petroleum ether, melted at 85° (according to data [4]: m.p. 87-88°).

Found %: N 26.91, 27.00. $C_2H_4O_3N_2$. Calculated %: N 26.92.

*Reaction of nitrogen tetroxide with potassium salt of nitromalonic ester.* To a suspension of 2 g of potassium salt of nitromalonic ester in 20 ml of dry ether there was added 1.5 g of nitrogen tetroxide (2 moles per 1 mole of ester salt) in 3 ml of dry ether. The reaction mixture turned brown and warmed itself to 25-30°.

The ethereal solution was filtered from potassium nitrate (0.84 g; quantitative yield) and was evaporated at 20°. In the residue remained 1.65 g of a colorless oil with a weak fruity odor. The oil was soluble in dilute alkalies and organic solvents but was insoluble in water; crystals formed on mixing this with a concentrated solution of potassium hydroxide; m.p. 154° (from alcohol). The mixed melting point with authentic potassium salt of nitromalonic ester gave no depression.

Thus, the oil formed in the reaction was nitromalonic ester (yield – 98.2%).

With the reactant ratio equal to unity, part of the initial salt does not react.

*Structure of potassium salt of nitromalonic ester.* The Raman spectrum of potassium salt of nitromalonic ester contained four very intense lines: 850, 1290, 1460 and 1710 $cm^{-1}$ and a weaker line – 1618 $cm^{-1}$.

Lines 850 and 1290 $cm^{-1}$ correspond to the nitro group in the normal form. Actually, in the spectra of all nitroalkanes one observes very intense frequencies in the regions of 830-900 $cm^{-1}$ and 1275-1385 $cm^{-1}$. These frequencies are absent in the spectra of salts of nitro compounds in which the nitro group is present in the aci-form. On this basis, among the two possible structural formulas of potassium salt of nitromalonic ester – (I) $KOON = C(COOC_2H_5)_2$ and (II) $C_2H_5OOC(NO_2) = C(OK)OC_2H_5$ – we must select formula (II).

The line 1618 $cm^{-1}$ must be assigned to the presence of the double bond $C = C$, while the line 1710 $cm^{-1}$ must be assigned to the carbonyl group $C = O$. The frequency 1460 $cm^{-1}$ belongs to the deformational vibration of the methylene link in the ethoxyl residue $OC_2H_5$.

## SUMMARY

1. In the reaction of nitrogen tetroxide with alkali salts of 2-nitropropane, ethyl ester of nitroacetic acid and 1,1-dinitroethane there are formed, respectively, propylpseudonitrole, ethyl ester of nitro-oximinoacetic acid and ethylnitrolic acid.

2. In the reaction of nitrogen tetroxide with the potassium salt of nitromalonic ester there is formed, quantitatively, the nitromalonic ester.

## LITERATURE CITED

[1] R. Scholl, Ber., 23, 3490 (1890).

[2] A. I. Titov and V. V. Smirnov, Doklady Akad. Nauk SSSR 83, 243 (1952).

[3] R. Scholl, Ber., 21, 506 (1888).

[4] M. Jovitschitsch, Ber., 28, 1213 (1895).

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## ERRATA

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| page | line | reads | should read |
|---|---|---|---|
| 718 | 4th from the top | $H_7[P(W_2O_7)_6] \cdot H_2O$ | $H_7[P(W_2O_7)_6] \cdot 4H_2O$ |

Vol. 28, No. 2 February, 1958

page 326, paragraph 4 (beginning with "An examination . . .") should read as follows:

An examination of the dissociation constants of the corresponding HX acids (which can be taken as a measure of the nucleophilic character of the anion $X^-$) shows that the weakest of the acids known to form ionic salts with tropylium is HNCO ($Ka = 1.2 \cdot 10^{-4}$) and that the strongest of the acids known to give covalent compounds with tropylium is HCN ($Ka = 7.2 \cdot 10^{-10}$).

# SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

| | |
|---|---|
| FIAN | Phys. Inst. Acad. Sci. USSR. |
| GDI | Water Power Inst. |
| GITI | State Sci.-Tech. Press |
| GITTL | State Tech. and Theor. Lit. Press |
| GONTI | State United Sci.-Tech. Press |
| Gosenergoizdat | State Power Press |
| Goskhimizdat | State Chem. Press |
| GOST | All-Union State Standard |
| GTTI | State Tech. and Theor. Lit. Press |
| IL | Foreign Lit. Press |
| ISN (Izd. Sov. Nauk) | Soviet Science Press |
| Izd. AN SSSR | Acad. Sci. USSR Press |
| Izd. MGU | Moscow State Univ. Press |
| LEIIZhT | Leningrad Power Inst. of Railroad Engineering |
| LET | Leningrad Elec. Engr. School |
| LETI | Leningrad Electrotechnical Inst. |
| LETIIZhT | Leningrad Electrical Engineering Research Inst. of Railroad Engr. |
| Mashgiz | State Sci.-Tech. Press for Machine Construction Lit. |
| MEP | Ministry of Electrical Industry |
| MES | Ministry of Electrical Power Plants |
| MESEP | Ministry of Electrical Power Plants and the Electrical Industry |
| MGU | Moscow State Univ. |
| MKhTI | Moscow Inst. Chem. Tech. |
| MOPI | Moscow Regional Pedagogical Inst. |
| MSP | Ministry of Industrial Construction |
| NII ZVUKSZAPIOI | Scientific Research Inst. of Sound Recording |
| NIKFI | Sci. Inst. of Modern Motion Picture Photography |
| ONTI | United Sci.-Tech. Press |
| OTI | Division of Technical Information |
| OTN | Div. Tech. Sci. |
| Stroiizdat | Construction Press |
| TOE | Association of Power Engineers |
| TsKTI | Central Research Inst. for Boilers and Turbines |
| TsNIEL | Central Scientific Research Elec. Engr. Lab. |
| TsNIEL-MES | Central Scientific Research Elec. Engr. Lab.—Ministry of Electric Power Plants |
| TsVTI | Central Office of Economic Information |
| UF | Ural Branch |
| VIESKh | All-Union Inst. of Rural Elec. Power Stations |
| VNIIM | All-Union Scientific Research Inst. of Meteorology |
| VNIIZhDT | All-Union Scientific Research Inst. of Railroad Engineering |
| VTI | All-Union Thermotech. Inst. |
| VZEI | All-Union Power Correspondence Inst. |

**Note:** Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. — Publisher.